Archives of Neurology and Psychiatry

VOLUME 54 SEPTEMBER 1945 NUMBER 3

STUDIES ON CEREBRAL EDEMA

I. REACTION OF THE BRAIN TO AIR EXPOSURE; PATHOLOGIC CHANGES

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It has been observed by neurosurgeons that in a certain number of patients undergoing large craniotomies involving exposure of the brain for long periods and cortical exploration there develop focal symptoms of paralysis, such as hemiplegia and aphasia, even when no cerebral substance has been removed. These symptoms appear within a few hours or one to two days after operation and are generally transitory, although they may persist in some cases for several weeks.

At Dr. Penfield's suggestion, Echlin [1] started a series of experiments to determine what effects on the brain or the meninges might be produced by operative exposure. He described lesions following simple exposure of the brain at operation which, from their nature and the similarity of their anatomic distribution to those produced by electrical stimulation, appeared to him to be due to cerebral ischemia. In those animals whose brains were exposed at operation for more than one hour he described adhesions between the leptomeninges and the pachymeninges, which appeared as early as the third postoperative day but when the dura was opened and immediately closed again, such adhesions did not occur except under the dura in the region of the silk sutures. He described also an inflammatory reaction in the leptomeninges, which disappeared eight days after operation. He found triangular areas of gliosis in the cat brains that had been exposed to air for two hours; the lesions were not prevented by protecting the brain from dry air with a glass covering or by irrigating continuously with solution of three chlorides U. S. P. at body temperature. He expressed belief that the gliosis was the result of a relative ischemia of the gray matter caused by compression of the pial blood vessels, which possibly was produced by the inflammatory exudate and adhesions that were shown to follow operative exposure of the brain.

Echlin's paper is interesting inasmuch as he attempts to give an explanation on an experimental basis of the aforementioned clinical findings. His conclusions are interesting enough to justify further investigation. We have repeated Echlin's experiments with a large series of animals and have followed closely the chronologic sequence of the cerebral reaction from the physiologic and the pathologic viewpoint.

In the present article we shall describe the pathologic observations made during and after the exposure, and in later papers we shall discuss the various physiologic changes.

MATERIAL AND METHODS

Cats were used in all our experiments. Aseptic technic was followed in all the exposure experiments. Anesthesia was obtained by the intraperitoneal injection of 0.6 grain (0.039 Gm.) of pentobarbital sodium per kilogram of body weight of the animal. A cranial incision was made in the midline, and the left temporal muscle was removed partially from its origin. An opening was made in the skull with a trephine and enlarged with rongeurs until it was approximately ¾ inch (1.9 cm.) in length and ½ inch (1.27 cm.) in width. The dura was gently lifted with a small curved needle and punctured with a small scalpel. A grooved director was gently inserted through the slit, and the mesial, the anterior and the posterior edge were cut. The dura was then carefully reflected laterally so that the brain was exposed in an area a little smaller than the size of the opening in the skull. The exposed area of the brain extended from the lateral sulcus down to the suprasylvian and middle ectosylvian gyri. The length of the exposure varied from four to seven hours. The dura was then closed with two silk sutures at each free corner. The galea and the muscle were then closed carefully. Sulfadiazine powder was placed on the suture and a small dressing applied to the wound; it was held there by means of liquid adhesive. The animals were killed by bleeding while they were under pentobarbital sodium anesthesia or with an overdose of pentobarbital sodium. They were killed immediately after exposure or at intervals of one, two, three, five and six days. In some cases solution of formaldehyde U.S.P., diluted 1:10, was injected into the brain after perfusion with isotonic solution of sodium chloride. The brains were fixed in formal solution of formaldehyde U. S. P., diluted 1:10, or in ammonium bromide-solution of formaldehyde or in alcohol. Blocks were cut on the freezing microtome or after embedding in paraffin or pyroxylin. The gold chloride (modified) method was used for astrocytes, and modifications of the Hortega silver carbonate technic, for oligodendroglial and microglial cells. Thionin and cresyl violet stains were used

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1. Echlin, F. A.: Cerebral Ischaemia and Its Relation to Epilepsy, Thesis, Faculty of Graduated Studies and Research, McGill University, 1939, p. 39.

for neurons in paraffin or pyroxylin sections. The hematoxylin-eosin stain or the Van Gieson and Weil method for myelin were also employed. The benzidine method was used for the vascular network.

RESULTS

Immediately after the opening of the dura the brain showed pulsating movements, which followed the respiratory rhythm. These movements stopped generally about two hours after exposure. At that time a certian degree of swelling of the brain substance was usually observed, as revealed by the bulging of the exposed area through the bone wound. The degree of swelling varied a great deal from one experiment to the other, and it depended on some factor the nature of which we are not yet able to determine. This swelling might reach such a degree as to make the closing of the dura impossible; a subsequent herniation, with injury of the brain substance, might take place. But as a rule the swelling was moderate and allowed the closing of the dura, although the edges could be brought into contact in only a few cases.

Vascular Changes.—Changes in the circulation were conspicuous a short time after the exposure. It is interesting to follow them in their chronologic sequence because they are of importance in explaining other functional and structural changes in the brain following the exposure.

As Echlin described, the meningeal vessels began to dilate about half an hour after the dura had been opened and the brain exposed. Dilatation was first seen in the veins, and for a while passive congestion was evident. This dilatation of the vessels gradually advanced until, by one and a half to two hours after the exposure, arteries as well as veins were dilated, engorged and prominent, and many vessels which were not visible to the naked eye became so during the exposure, the whole exposed area showing a diffuse pinkish blush.

Fig. 1.—Diapedetic hemorrhages in the brain twelve hours after exposure. Benzidine stain.

Postmortem examination of the brain at this time showed that this vasodilatation, although much more prominent over the exposed area of the brain, extended over the entire brain, including the vessels of the diencephalon. In coronal sections of the brain one could see numerous red cells in the subarachnoid spaces and in the ventricles, mainly the third, and in the infundibulum. On microscopic examina-

tion of the brain stained by the benzidine method definite engorgement of the large vessels was found, more prominent in the veins than in the arteries. Under a low power lens, one noticed a very irregular distribution of the blood in the capillary network and patches of empty or collapsed capillaries, especialy around the large vessels. Small perivascular hemorrhages could be found through the whole brain, in the gray as well as in the white matter (fig. 1), along the periventricular region, in the periventricular gray matter of the third ventricle and in the

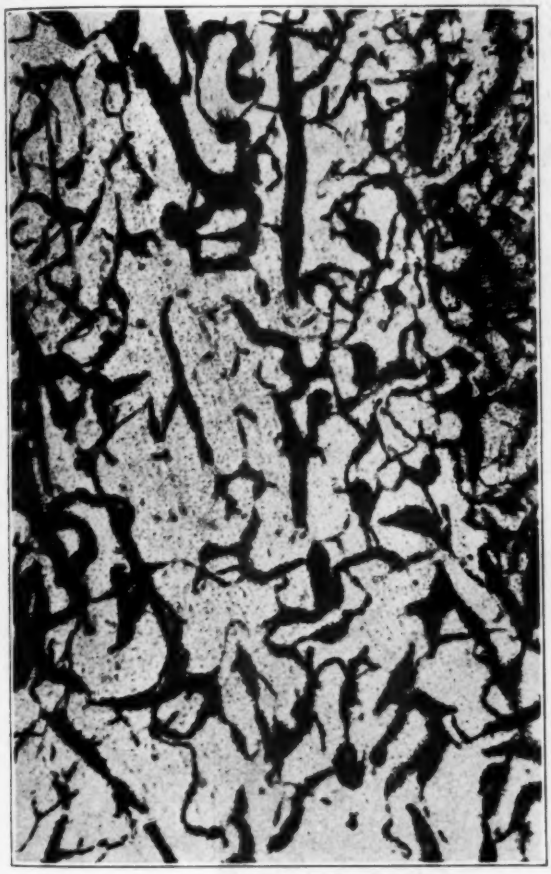

Fig. 2.—Capillaries of the white matter of the brain twenty-four hours after exposure. Benzidine stain.

tuber cinereum, where the vessels seemed to dilate and become engorged to a conspicuous degree. Capillaries (fig. 2) and small vessels showed either dilatation and stasis or were empty and irregular in shape. Many of these vessels showed the formation of slight bulging or small aneurysm-like widenings, which indicated loss of tonicity of the wall. In most of the cases the hemorrhages were only diapedetic. Real hemorrhages, with loss of continuity of the wall of the vessel, were rare and were consistently present only when the swelling was pronounced and herniation of brain substance took place. In these cases large hemorrhages could be found in the exposed area and its vicinity and were conspicuous in the white matter.

If the animal was killed twenty-four hours after the exposure, the picture changed somewhat (fig. 3). The meningeal vessels were still engorged with blood. The brain, however, in many places showed definite signs of ischemia. Many arteries were dilated and distended and contained little or no blood, but the veins still showed stagnation and irregular dilatations to a considerable degree, especially in the deepest layers of the gray matter and in the white matter, where the venous stagnation seemed to be at its height. Extravasated red blood cells had mostly disappeared and could be seen only in places where the hemorrhages were larger. The perivascular spaces were now very wide. Many of the capillaries were collapsed. The nuclei of the endothelium were pyknotic, and the protoplasm of the cells might show vacuolation. Occasionally small vessels or capillaries exhibited dilatations, filled with red blood cells. Rarely, however, the endothelium showed actual breaks, although in a few isolated instances one could even see retractions of the vessels at both ends and accumulation of blood cells in the perivascular space.

On the third day the ischemic patches of the cortex began to be less evident, and the normal circulation seemed to be reestablished. Dilatations of the veins and of some arteries still persisted, especially in the deep layers of the gray matter and in the white matter, showing that their walls had been damaged somewhat and had lost their tonicity.

On the fifth day after the exposure (fig. 4) benzidine staining of the brain showed a normal picture except for a few bulges or aneurysm-like widenings of some vessels. The perivascular spaces had come back to their normal appearance.

Cellular Changes.—Two types of neuronal changes were observed: (*a*) swelling and chromatolysis, and (*b*) shrinkage and homogenization. Although these alterations correspond with the classic descriptions made by histopathologists, we prefer to describe them as they were found in our slides.

Swelling and Chromatolysis: In the swollen cells (fig. 5) the protoplasm was lightly stained, and its processes were swollen and not clearly seen; many of these cells, however, did not show any processes at all and were round or irregular in shape. The cytoplasm of the cell body might show numerous vacuoles, which gave it a sponge-

like appearance. The substance was completely absent or was diffuse, dustlike and generally displaced to the periphery. The nucleus was large and swollen, with little or no chromatin; it was displaced in many instances to the periphery but frequently occupied almost entirely the whole cell body, occasionally being partially surrounded by a small zone of deeply stained cytoplasm. The nucleus in most cases was perfectly round, but in many instances the nuclear membrane was shrunken and the nucleus irregular in shape. The vacuoles in the cytoplasm seemed to push the nucleus in many directions, contributing to its irregular form. The nucleolus was large, rounded and deeply stained. In some cases the cellular membrane seemed to have burst, and no protoplasm was seen around the nucleus, which appeared to be the only remaining cellular structure. In other instances, a very pale, unstained silhouette or irregular outline, without any structure, was all that remained of the cell.

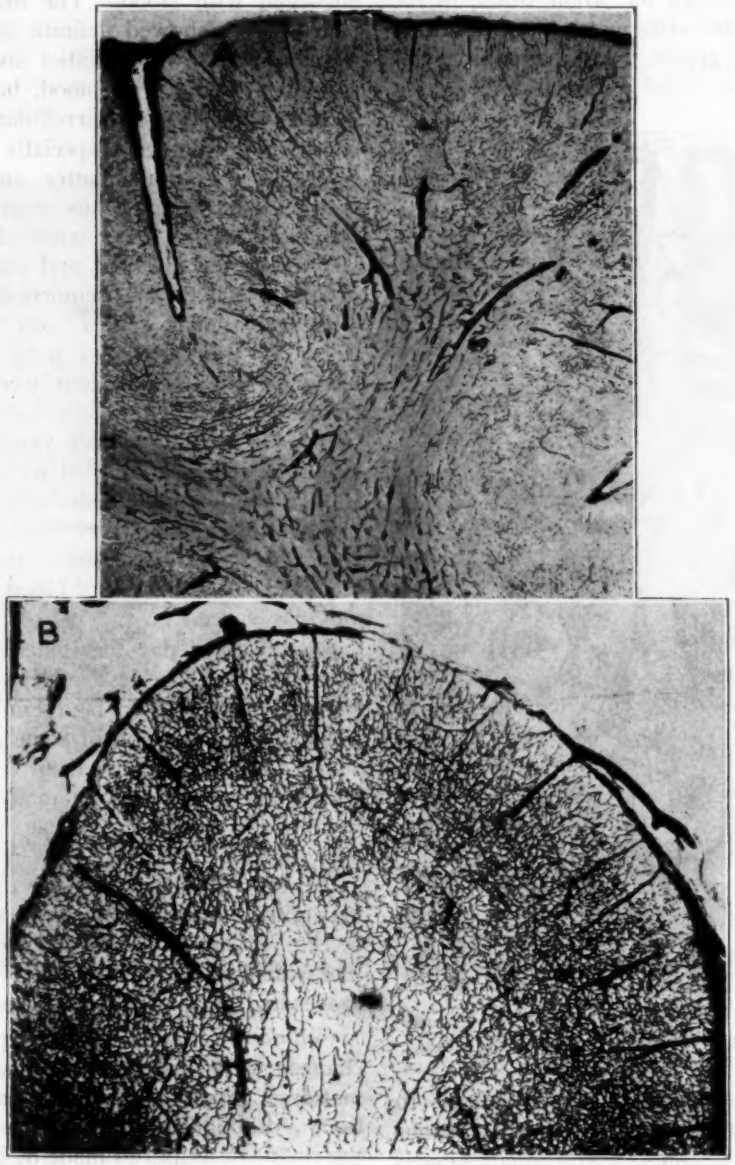

Fig. 3.—*A*, cerebral cortex, showing ischemia of the gray matter and engorgement of the deep vessels twenty-four hours after exposure. *B*, normal cerebral cortex of the cat. Benzidine stain.

Shrinkage and Homogenization (fig. 6): The neurons were shrunken and darkly stained, with angular corners; concave depressions appeared in the sides of the cell body, the shrinkage affecting only the diameter of the cell, and not its length. In fact, the cell might actually show

an extraordinary degree of elongation. The pale-stained processes were wavy and crinkled and could be followed for some distance from the cell body. Only the cell body was dark. The nucleus was irregular in shape and usually elongated, like the cell body, its outline not being very clear. A dark-stained nucleolus could almost always be seen, and usually quite in the center of the nucleus. The cytoplasm was stained homogeneously dark blue (thionin), although darker masses could be seen sometimes around the nucleus, making difficult the determination of its outline. These dark masses patches of ischemia, the shrinkage and homogenization were more in evidence.

These neuronal alterations were not exclusively localized to the exposed area. Indeed, they could be seen as well in both hemispheres throughout the whole brain, including the subcortical structures at the base of the brain. They were, however, more conspicuous in the more caudal and ventral regions of the cortex, chiefly in the lobus pyriformis, the occipital pole and the cornu ammonis. The lobus pyriformis on each side was without any doubt the region that showed the largest number of altered cells.

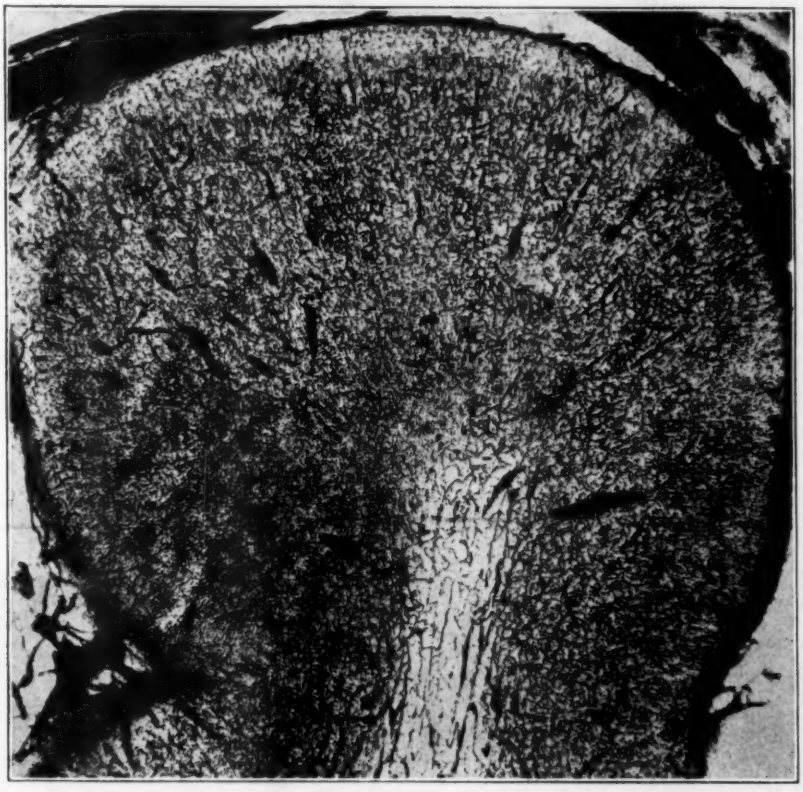

Fig. 4.—Cerebral cortex five days after exposure, showing reestablishment of the circulation. Dilatation of some deep vessels still remains. Benzidine stain.

stopped sharply at the origin of the processes, which remained lightly stained. With the silver carbonate method, the same picture could be seen, although the cytoplasm was uniform and pale, and the nucleus, which was sharply seen, was very dark.

The degree to which these cellular alterations appeared in the brain seemed to depend on the length of time which had elapsed since the exposure. Immediately after the exposure swelling and chromatolysis predominated. This cellular change was still frequently seen during the next twenty-four hours, although by that time, when the benzidine method revealed prominent

Swollen cells became rarer twenty-four hours after exposure, and shrunken, homogeneous cells dominated the picture. Zones or areas of devastation could already be seen, indicating that some of these swollen cells had undergone complete disintegration. However, many swollen cells could still be seen in the deeper layers of the cortex, whereas in the more superficial layers most of the cells showed shrinkage and homogenization. Forty-eight hours after exposure the latter alteration was the only type found, chromatolysis and swelling no longer being present. At this time the histologic picture of the cortex was characteristic (fig. 7). The larger vessels

were still engorged and filled with blood cells. The perivascular spaces of both large and small vessels were prominent and very wide, as were the perineuronal spaces of the shrunken neurons. A few swollen cells and zones of devastation completed this picture of a mild but evident edema-like condition. By the third and fourth days the histologic picture began to return to

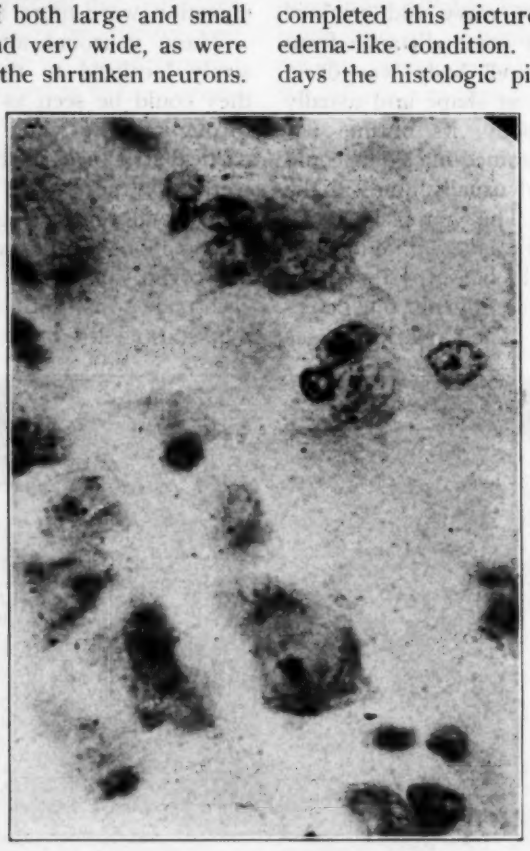

Fig. 5.—Neurons of the cerebral cortex, showing acute cellular alteration. (See text.) Nissl stain.

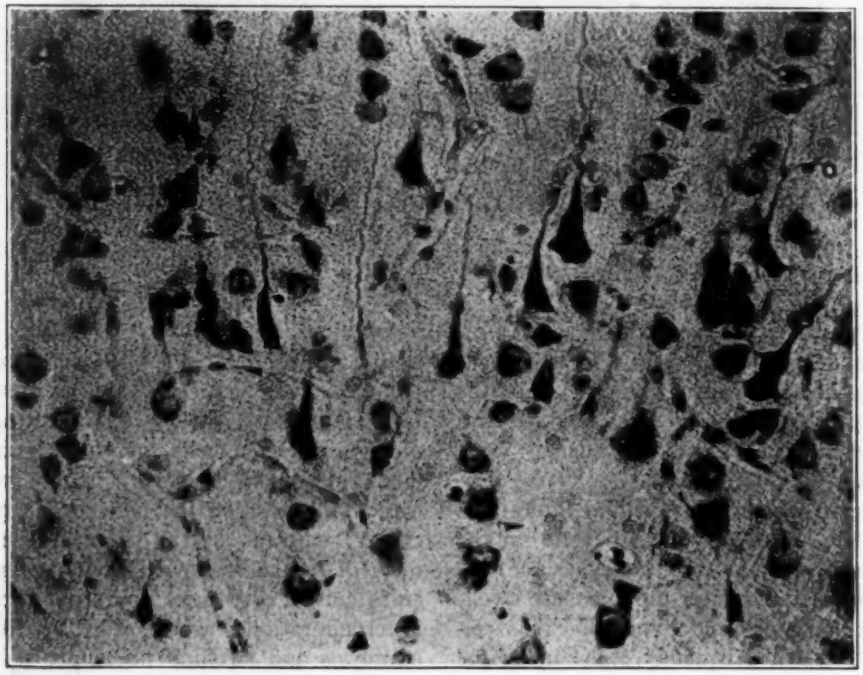

Fig. 6.—Cerebral cortex, showing different types of neuronal alterations following exposure (for twenty-four hours). (See text.) Nissl stain.

normal in most of the regions of the brain except the lobus pyriformis, which still showed the shrunken neurons. Isolated small groups of shrunken cells might be found, however, for a few days, but they were no more frequent than was usually seen in the control animals.

Interstitial Cells.—Of the three types of interstitial cells, only the oligodendroglia cells remained completely normal. Astrocytes and microglia cells showed changes of varying kind and degree, according to the length of time after the exposure.

As might be expected, the cells that showed the earliest changes were the microglia cells (fig. 8); indeed, such changes appeared within twenty-four to forty-eight hours after the exposure. Although microglial cells react rapidly and with moderate intensity, this reaction was temporary. Both progressive and regressive changes were seen simultaneously. There was an increase in size which affected both the processes and the cell body; the dendrites were thick, with sharp contour, beset with spines and of angular outline; the delicate small branches had disappeared, so that the cells exhibited only their more primary branches. Cells adopting the so-called rod shape, as well as elongated cells, were seen, although the former were very scarce. The cell body appeared swollen and showed a coarse reticulated structure. The nucleus was small, pyknotic and displaced; granules of different sizes and shapes at times occupied almost the whole body. In a later stage the processes became thinner and broke up, whereas the cell body continued to swell, until finally it might "explode." Compound granular corpuscles, however, were never seen, but a certain mobilization of the affected cells was present, as demonstrated by the fact that around the vessels, and even in their perivascular spaces, were cells which seemed to discharge their stored granules into the capillaries. After the fourth day, however, microglial cells might show slight changes in isolated areas but for the most part were entirely normal.

Astrocytes.—Little or no change was seen in the neuroglia during the first days after the exposure. In some cases, however, it seemed that the exposed area of the cortex showed hyperplasia of both types of astrocytes, which was more marked in the supragranular layer and in the marginal neuroglia. Later, about the fifth or the seventh day, a true gliosis might appear. Not only was there an increase in the number of gliocytes, but hypertrophy of both body and processes might be present. No protoplasmic neuroglial cells were seen, all being of the fibrous type, with very thick processes. As Echlin showed, this gliosis was particularly noticeable in the marginal neuroglia of the exposed area but invaded as well most of the gray matter and even the underlying white matter. It may be interesting to point out that acute regressive changes were never seen at any moment, even on the first day after the exposure. The changes observed were only pro-

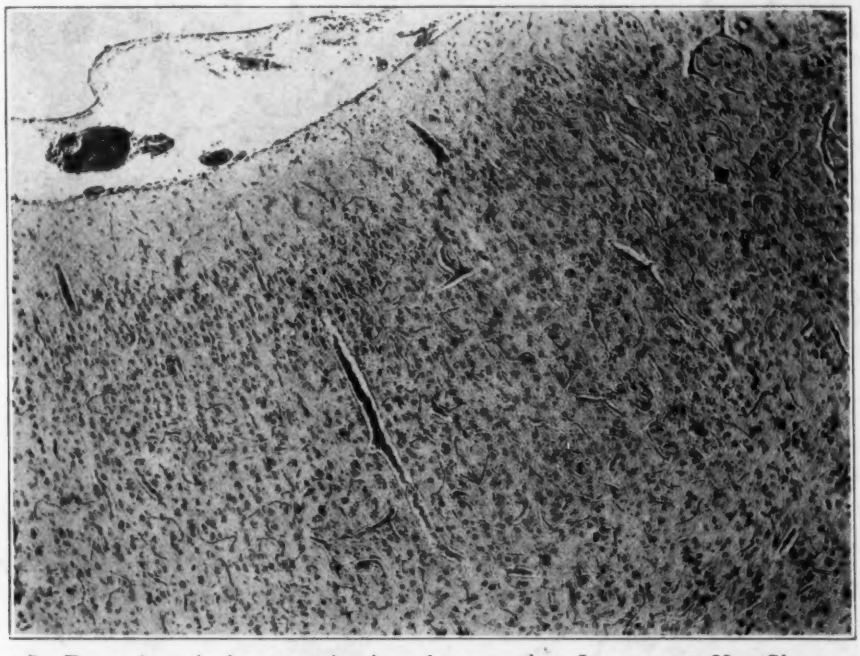

Fig. 7.—Exposed cerebral cortex, showing edema reaction. Low power; Van Gieson stain.

gressive in nature and were certainly reactive to circulatory alterations.

Blood-Brain Barrier.—The histologic picture already described showed us clearly that as a result of the exposure to the air of a limited area of the cat brain there develops a generalized reaction of the whole brain, which disappears almost completely after six to seven days. This reaction affects primarily the vessels, with the result that there is an increase in the outflow of fluid from the vessels into the tissue spaces. The numerous diapedetic hemorrhages and the bulging and aneurysm-like dilatations of capillaries show that the permeability and tonicity of the capillary endothelium are altered.

In order to ascertain to what extent the permeability of the blood-brain barrier was affected during the exposure, the behavior of solutions of trypan dyes on intravital injection was observed.

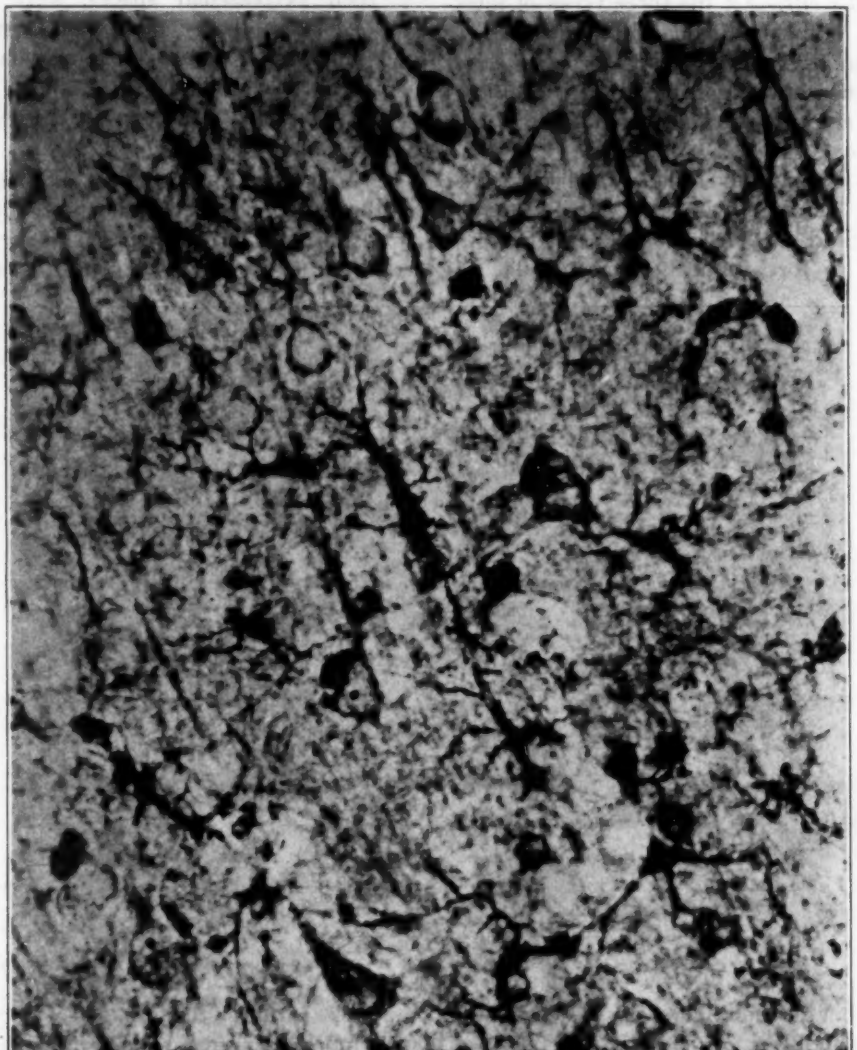

Fig. 8.—Slight microglial reaction twenty-four hours after exposure. Silver carbonate stain.

Goldmann [2] first demonstrated the fact that solutions of trypan blue, when injected into experimental animals, stain all organs of the

2. Goldmann, E. E.: Vitalfärbung am Zentralnervensystem, Berlin, G. Reimer, 1913.

body diffusely except the leptomeninges and the brain, which remain "snow white," to use the expression of the aforementioned investigator. Only limited and specific structures of the brain are stained, i. e., the chiasmic region, the tuber cinereum and pituitary body, the choroid plexuses and the area postrema. These experiments, widely confirmed later by numerous investigators, gave clear evidence for the first time of the presence of what has since been called the blood-brain barrier. This implies that the permeability of the endothelium of the capillaries of the brain is more selective than that of the capillaries of most other organs, at least for certain kinds of colloidal solutions, such as the trypan dyes.

From 10 to 20 cc. of a 1 per cent aqueous solution of the dye was injected into our animals at the end of the exposure. The injection was

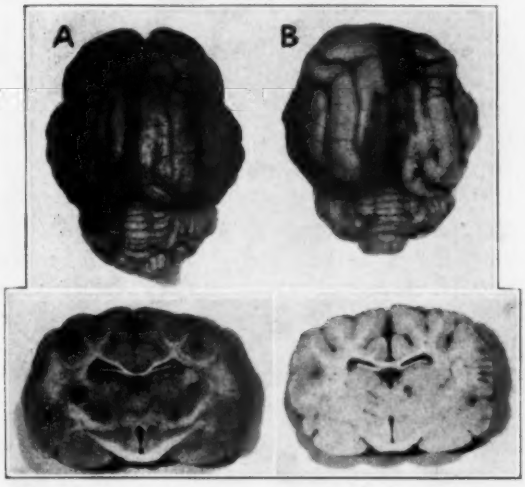

Fig. 9.—Increased permeability of the cerebral capillaries following exposure. *A*, brain of a cat into which 20 cc. of a solution of trypan red was injected immediately after the exposure and the animal killed twenty-four hours later. *B*, brain of a control animal, in which the same solution was injected, but no exposure was performed. Only the dura is stained.

repeated the following day and the animal killed a few hours later. Postmortem examination of the brain (fig. 9) showed that the whole cerebrum was slightly but definitely stained by the dye. The exposed area, however, was much more darkly stained, so that it was clearly outlined from the rest of the cortex. The gray matter was more stained than the white, owing to the greater number of vessels. The choroid plexuses, the tuber cinereum and pituitary and the area postrema were all darkly stained. The anterior part of the brain (cortex) was paler than the posterior, and, as a rule, the base was paler than the convexity. In coronal sections of the brain one could see that the staining was not quite uniform but that patches of darker color spread out, without following any characteristic distribution. The subcortical structures —the striatum, the thalamus and the hypothalamus—might in some cases be rather deeply stained, especially those in which the swelling of the brain was obvious. The blue color of the brain disappeared almost completely in the sections cut for histologic examination, even if they were very thick. Interestingly, not much of the dye could be seen inside the vessels (and most of them did not have any at all). This is important, since Spatz,[3] in his experiments with massive intravital injections of trypan blue in rabbits, described a light blue tinge of the brain which he concluded was due to the presence of the dye inside the capillaries. However, in the illustrations he showed the capillaries in blue, whereas the cerebral substance was quite unstained. Examination under an immersion oil lens of thin, unstained sections of the brains of our animals showed many minute granules of the dye scattered throughout the brain, around the vessels, in the perivascular spaces and even inside the cells. The scanty amount of blue which remained inside the vessels and the presence of these granules in the brain tissue are evidence of the passing of the dye across the capillary endothelium.

Von Möllendorff's studies[4] with intravital injections of trypan blue demonstrated first that ectodermal elements of the brain—neurons and both types of neuroglial astrocytes and oligodendroglial cells—do not have any affinity for the dye except in conditions of damage. He found minute granules of trypan blue in the cytoplasm of only the damaged neurons and neuroglial cells; dead cells were diffusely stained; well preserved, undamaged cells, however, remained completely unstained. Later, King[5] demonstrated again the lack of affinity of the ectodermal cells for the trypan blue on this basis, and he questioned the existence of the blood-brain barrier.

Our studies showed that to a certain extent neurons can retain small amounts of trypan granules if they are damaged or swollen, but we failed to see any dye at all in the apparently

3. Spatz, H.: Die Bedeutung der vitalen Färbung für die Lehre von Stoffaustausch zwischen dem Zentralnervensystem und übrigen Körper, Arch. f. Psychiat. **101**:267, 1934.

4. von Möllendorff: Vitale Färbung an tierischen Zellengrundlage: Ergebnisse und Ziele biologischer Farbstoffversuche, Ergebn. d. Physiol. **8**:141, 1920.

5. King, L. S.: The Hematoencephalic Barrier, Arch. Neurol. & Psychiat. **41**:51 (Jan.) 1939.

normal cells. In slides stained with silver carbonate methods, we could follow the behavior of the microglial cells. It is out of the realm of this paper to discuss cytologic problems concerning this interesting question. Suffice it to say that microglial cells become activated as a result of the exposure because they have to phagocytose red blood cells, and probably products from disintegrated neurons. But when, in addition, the trypan blue is injected, the degree

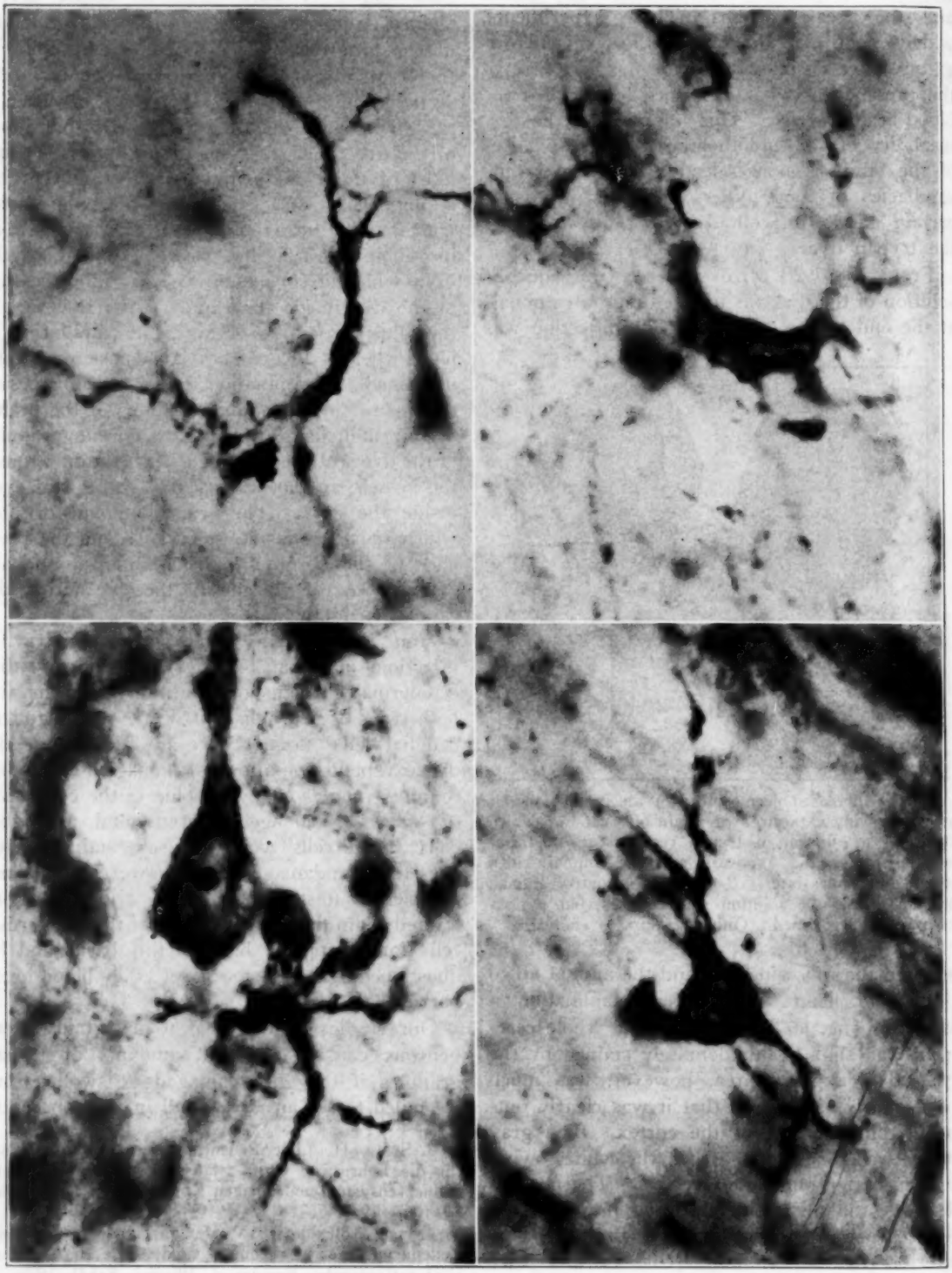

Fig. 10.—Different types of microglial cells of the brain of a cat following exposure and injection of trypan blue, showing phagocytic activity. Silver carbonate stain.

of activity is more manifested (fig. 10). Large, dark granules are seen inside the body of the microglial processes. No doubt some of these granules represent debris of the blood cells and other products of disintegration resulting from the circulatory alterations, but most of them are stored-up precipitate of the trypan dye. Since our first experiments, we have been impressed by the fact that many more and thicker granules were seen in the slides stained with the silver carbonate methods than in either the unstained sections or the sections stained simply with carmine. Further in vitro experiments convinced us later that the silver carbonate solution precipitates the colloidal trypan solution in coarse, dark granules; this explains the difference between the picture observed in the unstained sections and that in sections stained with the metallic methods. In the latter we always could see a larger number of coarse granules, both in the intercellular spaces and in the cells, than in the former. This was also particularly evident inside and around the vessels, where granules could be seen with the silver technic which were absent in the carmine-stained or in the unstained sections. Apparently, the lack of affinity of the ectodermal elements for the trypan dye resulted in most of the solution being maintained in a colloidal state until the later presence of the silver carbonate altered it and helped the formation of the coarse precipitate.

COMMENT

Spielmeyer [6] first investigated the pathologic changes in the brains of patients dying of various forms of vascular disease which were supposed to produce cerebral anemia. He described various types of neuronal alterations in the cortex which he considered characteristic of cerebral ischemia. The cellular changes were characterized by swelling, shrinkage, liquefaction or coagulation of the neuron, each one of them giving a more or less typical histologic picture. A few years later, Gildea and Cobb [7] produced cerebral anemia experimentally in cats and studied the brains microscopically. All cats in which symptoms of pronounced cerebral anemia developed showed lesions in the cerebral cortex. The neurons were characteristically shrunken and darkly stained with irregular nuclei. Swollen cells and chromatolysis were also found when the anemia was sufficiently complete. Areas of devastation, showing absence of many cells and interrupting the normal orderly lamination, were frequently observed. Although these focal areas of necrosis required at least twenty-four hours to appear, shrinkage, chromatolysis and homogeneous staining of the cells appeared immediately after prolonged anemia. This work confirmed the postmortem studies by Spielmeyer on the human brain and supported his view that the morphologic changes were due to ischemia.

In our studies, the types of cellular alteration corresponded with the description by these investigators. We observed, as did Gildea and Cobb, that shrinkage and homogeneous staining of the cells were much more conspicuous and more frequent than chromatolysis, swelling and liquefaction and that no correlation existed between the clinical condition of the animals and the pathologic changes in the cells. In our opinion, the ischemia observed after the dilatation which followed the exposure is sufficient to account for these cellular changes. The increase of permeability of the capillary endothelium demonstrated by the diapedetic hemorrhages and the trypan blue experiments explains the increase in the bulk of brain tissue as a result of the abnormal accumulation of fluid in the cerebral parenchyma. Certainly, the degree of increase in volume of the brain varies a great deal from one experiment to another. On the other hand, the histologic picture of the cellular and vascular changes, with the conspicuous widening of the Obersteiner and the Virchow-Robin spaces, presents a more constant feature. Circulatory changes are, therefore, the most important factor from a pathogenic point of view in the reaction of the brain after exposure.

The pathologic picture of edema of the brain is described as rarefaction and hydration of the tissue spaces, which give the brain an areolar, honeycombed appearance, dilatation of the perigangliónic and perivascular spaces and increase in the protoplasmic astrocytes, which may show also a tendency to ameboid degeneration. Recent investigators have stressed the importance of circulatory changes in the pathogenesis of edema. Scheinker [8] stated that the histologic picture of cerebral swelling includes morphologic signs of vascular alterations, with an increase in the permeability of the vessel walls, widening of the perivascular and perineuronal spaces by outflow of fluid from the vessels, areolar appearance of the tissue, vascular stasis

6. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

7. Gildea, E. F., and Cobb, S.: The Effects of Anemia on the Cerebral Cortex of the Cat, Arch. Neurol. & Psychiat. **23**:876 (May) 1930.

8. Scheinker, I.: Cerebral Swelling and Edema Associated with Cerebral Tumor: Histogenetic and Histopathologic Study, Arch. Neurol. & Psychiat. **45**: 117 (Jan.) 1941.

and diapedesis. He concluded that vascular alterations are the fundamental features in the genesis of the swelling and that the difference between edema and swelling is only a matter of degree, the edema showing morphologic changes in the vessels which are not found with swelling.

Greenfield [9] also did not accept the view (held by Spatz and others) that edema and swelling are different processes. With the edema accompanying brain tumors he described degeneration of the myelin and swelling and varicosities in the myelinated axons, swelling of astrocytes and moderate activation of the microglia. He expressed the belief that the presence of an excess of interstitial fluid interferes with the adequate diffusion of oxygen from the vessels to the cells.

Nieto and Caso (cited by Obrador Alcade [10]) in experimental acute swelling of the dog brain failed to find any morphologic changes in the neurons or in the interstitial cells, myelin and axons also being apparently normal. Only the widening of the perivascular spaces was evident.

Our experiments show that the vessels of the brain undergo an increase in permeability and certain morphologic changes which would lead us to agree with Scheinker's point of view that the circulatory changes are essential to explain the excess of fluid in the tissue spaces which is the fundamental feature in any edematous condition.

Finally, our experiments demonstrate also that in a strict sense the increase in the brain bulk cannot be accepted as *conditio sine qua non* for the diagnosis of cerebral edema. Only when the amount of interstitial fluid is exaggerated will the volume of the brain be increased. In milder reactions, such as those in most of our exposure experiments, one sees only the histologic picture of edema without much change in the volume of the brain.

SUMMARY AND CONCLUSIONS

When an area of cerebral cortex in one hemisphere of the cat brain is exposed to the air for several hours, an acute reaction of brain tissue takes place which persists up to the fourth or fifth day after closure of the exposure wound.

This reaction is more severe in the exposed area but is also evident in more remote regions of both hemispheres and in the subcortical structures. It is characterized by both circulatory and cellular changes.

Grossly, the circulatory changes appear first as a brief period of venous dilatation and engorgement, followed by active congestion due to arterial dilatation, which reaches its maximum about two hours after the beginning of the exposure, at which time the pulsating movements of the brain with respiration disappear and some cerebral swelling may be noticeable. The degree of this swelling varies greatly from one experiment to another: In some cases an actual herniation of the exposed area is present, whereas in others the increase in volume is scarcely perceptible.

Microscopic examination of sections shows scattered diapedetic hemorrhages throughout both hemispheres in the gray and white matter and in the subcortical structures. They are, however, more conspicuous in the exposed area. If the degree of cerebral swelling is very pronounced, actual hemorrhages, with loss of continuity of vessel walls, are seen. Twenty-four hours after the exposure, areas of ischemia are present throughout the whole cortex, particularly in the exposed area; veins are still dilated and engorged, but some arteries are empty. The capillaries are collapsed and empty, or they may show engorgement with blood cells. The perivascular spaces are extremely distended, and the permeability of the capillary endothelium is increased. Three days after the exposure, the circulation is practically reestablished; a few vessels may still show aneurysm-like dilatations where their damaged walls have not yet recovered.

The cellular changes appear early and are characterized by swelling and chromatolysis or shrinkage and homogenization. Some neurons undergo complete destruction, and occasional zones of devastation can be seen. As with the circulatory changes, the neuronal alterations also clear up by the third day after exposure, and, except for the permanent destruction of a few neurons, the histologic picture at that time may be completely normal. Microglial cells show a mild reaction of brief duration, which is, however, more evident when trypan dyes have been injected. The neuroglia gives only slight response to the exposure. This is manifested by moderate hyperplasia, followed by gliosis confined mostly to the exposed area, especially in the pial neuroglia, which may be the only region where any visible neuroglial change remains. The oligodendroglia shows no change whatever.

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9. Greenfield, J. G.: The Histology of Cerebral Edema Associated with Intracranial Tumors (with Special Reference to Changes in the Nerve Fibers of the Centrum Ovale), Brain **62**:129, 1939.

10. Obrador Alcalde, S.: Cerebral Edema, An. méd. **3**:31, 1942.

TREMORS OF COMBAT NEUROSES

COMPARISON WITH TREMORS OF PARALYSIS AGITANS, DELIRIUM TREMENS AND THE PSYCHONEUROSES OF CIVILIAN LIFE; ELECTROMYOGRAPHIC STUDIES

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The acute neuroses of war are in many ways unlike any syndromes seen in peacetime civilian life. In World War II the first severe neuroses were seen in the men evacuated from the beaches at Dunkerque. These men showed several outstanding symptoms, many of which have since been described in the literature. They had all been exposed to severe strain; all were exhausted and dehydrated and in most cases had had no sleep for four days. In addition to the trial of physical endurance, they had been in continuous danger of death and had been exposed to the repeated trauma of seeing men die violent deaths.

One frequent symptom was a gross tremor, usually of the hands, and in many cases this tremor was so marked that the diagnosis of paralysis agitans was in question. This diagnosis was supported by the facies, which was often masklike in its listlessness and apathy. In the course of another line of investigation, which included observations on the arm, one characteristic of these tremors was very striking, and this is the subject of the present paper. In these patients the tremor often appeared to be a rhythmic jerking of the whole limb without the alternation of flexion and extension seen in tremors of paralysis agitans. Unfortunately, no electromyograph was available at that time in the hospital in which these patients were being studied (Sutton Emergency Hospital, England).

In the electromyographic laboratory at the Massachusetts General Hospital it has now been possible to make electromyographic studies of similar tremors in cases of combat neuroses. All the subjects studied were patients from the United States Naval Hospital at Chelsea, Mass., and the investigation was undertaken under a project from the Bureau of Medicine and Surgery of the United States Navy (Project No. X369 Gen. 54).[1]

Although a longer period had elapsed between the combat experience and the examination of these men than occurred in the case of the Dunkerque survivors, tremor was still an outstanding symptom.

The purpose of this study was an attempt to use the electromyograph in making a differential diagnosis of tremors due to lesions of the extrapyramidal system, tremors of psychogenic origin and tremors due to metabolic disorders or drug intoxications. The tremors of basal ganglia origin are usually classified in three groups: tremors due to degeneration in the basal ganglia consequent to arteriosclerosis in senile persons; tremors due to lesions which are the sequelae of encephalitis, and post-traumatic tremors presumably associated with some lesion in the basal ganglia, such as damage to small blood vessels. Because of the age range of these service men, the last two types only need be considered.

METHOD

For the recording of electromyograms, a three channel ink-writing oscillograph, such as is standard for electroencephalographic technic, was generally used, although in some cases in which simultaneous multiple recordings from many muscles were required, a six channel machine was employed. Since in this study the interest lay in the behavior of the muscle as a whole rather than in the single motor unit, the electrode technic used consisted of the employment of small, flat solder disks, approximately 1 cm. in diameter, pasted on the skin over the belly of the muscle under observation. The currents from the muscles were amplified in the usual manner, the electromyographic technic being in general similar to that described in other studies of muscle potentials.[2]

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This study was aided by a grant from the George Harrington Trust Fund.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

1. Lieut. Comdr. Herbert I. Harris (MC), U.S.N.R., furnished the clinical histories of the Navy personnel used in this study. Dr. Harris left for duty overseas before the electromyographic data were worked up, and he is therefore not responsible for any opinions stated in this paper.

2. Schwab, R. S.; Watkins, A. L., and Brazier, M. A. B.: Quantitation of Muscular Function in Cases of Poliomyelitis and Other Motor Nerve Lesions, Arch. Neurol. & Psychiat. **50**:538-545 (Nov.) 1943.

Previous work in this laboratory, in collaboration with Comdr. Robert S. Schwab (MC), U.S.N.R., and in other laboratories has established certain characteristics of the tremor of paralysis agitans. This tremor is usually in the frequency range of 4 to 7 cycles per second and is of great regularity in any one patient; Schwab and Cobb [3] have shown the maximum variation in any one muscle group to be 10 per cent, but it is commonly much less than this. The form of the electrical potentials is also characteristic, being a smooth build-up to a maximum spike followed by a smooth decrease to relaxation, with a period of comparative quiet between the individual tremor bursts. An example of the tremor of paralysis agitans is shown in figure 1.

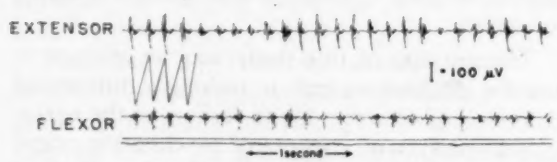

Fig. 1.—Tremor in a case of paralysis agitans (case 4, table 2). Note the regularity of pattern and frequency and alternation of the tremor bursts from extensor to flexor muscle.

Another characteristic of the tremor of paralysis agitans demonstrable by the electromyogram is that when simultaneous recordings are made from opposing muscles at rest, as, for example, from the extensors and flexors of the forearm, the tremor potentials are out of phase in the antagonistic muscles (fig. 2). The alternation

Fig. 2.—Tremor in a case of paralysis agitans. The tracing has been enlarged to demonstrate the alternation of action potentials from agonist to antagonist muscle.

of flexion and extension is well known and produces the typical pill-rolling movement of paralysis agitans. It is not to be confused with the opposite phenomenon of disordered reciprocal innervation present in rigid muscles on voluntary movement. This has been described by Hoefer and Putnam.[4]

3. Schwab, R. S., and Cobb, S.: Simultaneous Electromyograms and Electroencephalograms in Paralysis Agitans, J. Neurophysiol. **2**:36-41, 1939.

4. Hoefer, P. F. A., and Putnam, T. J.: Action Potentials of Muscles in Rigidity and Tremor, Arch. Neurol. & Psychiat. **43**:704-725 (April) 1940.

These three characteristics of the electromyogram of the tremor of paralysis agitans formed the nucleus for observation on the tremor of combat neurosis—that is, the frequency, the electromyographic pattern and the alternation in opposing muscles at rest.

RESULTS

In this series, 23 cases of tremor among service personnel were investigated. In 3 of these 23 cases the neurologic examinations gave evidence of tremor of postencephalitic paralysis agitans, and they are omitted from the classification of combat neurosis. These 3 cases will be presented in detail later, but in brief summary it may be said that in each of these cases the tremor had a frequency of 6 to 7 cycles per second and showed extreme regularity. The bursts in the extensors and the flexors were out of phase, and at no time did they occur synchronously.

In the other cases in which the diagnosis was combat neurosis, no tremor slower than 8 cycles per second was found. Synchrony between opposing muscles was common, and in some cases spontaneous diphasic spikes were found in the

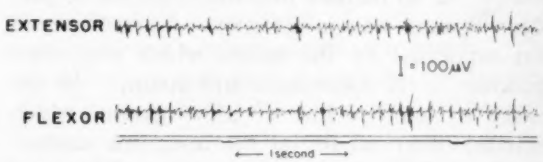

Fig. 3.—Tremor in a case of combat neurosis (case 13, table 1). Note the fast frequency, the irregularity of the bursts and the frequent synchrony between opposing muscles.

resting muscles. The cases have been briefly summarized in table 1, and a typical electromyogram of a tremor of psychogenic origin (case 13) is shown in figure 3.

Study of table 1 gives several items of information about the tremors in these cases. It will be noticed that whereas all the cases in the table are classified under the diagnosis in current Naval usage, i. e., combat neurosis, there is made in the fourth column some slight breakdown of this overall diagnosis from the patient's symptoms and history.

A brief description of the type of tremor is given in the fifth column, and in the sixth column is a note as to alternations of the tremor from agonist to antagonist groups.

When one looks for the characteristics which have been listed as typical of the electromyograms of the tremor of paralysis agitans, they are conspicuously absent in this series, with the single exception of case 14. In the first place,

the frequency of the tremor is often so fast as to give a completely diffuse electromyogram, with no discernible rhythm; the clearcut pattern of the rhythmic muscle discharge seen in the tremor of paralysis agitans is entirely absent (compare, for example, figures 2 and 3 with figure 1). There are also no clear interspaces between the tremor bursts (again, with the exception of case 14). Finally, there is no alternation of the tremor from flexor to extensor groups, with, once more, the exception of case 14.

TABLE 1.—*Electromyographic Data on Tremor in Cases of Combat Neurosis*

Case No.	Patient	Age	Diagnosis	Type of Tremor	Presence or Absence of Synchrony in Antagonists
1	M. K.	29	Anxiety neurosis with chronic tremor since age of 12	On extension only; 8-10 per sec.	No tremor in flexors
2	W. P.	26	Acute anxiety state	Very gross, diffuse and irregular; no clear interspaces	Diffuse tremor in antagonists
3	M. Q.	35	Anxiety neurosis; many early psychoneurotic traits	Diffuse with no definite frequency; no clear interspaces	Diffuse tremor in antagonists
4	C. V.	30	Psychoneurosis neurasthenia	Mostly diffuse, never slower than 10 per sec.; no clear interspaces	Often synchronous
5	J. S.	33	Anxiety neurosis in a constitutional psychopath	Diffuse tremor in extensors; no clear interspaces	Diffuse tremor in antagonists
6	B. P.	29	Hysteria	8-9 per sec.; no clear interspaces	Asynchronous
7	E. M.	22	Anxiety neurosis	Gross spasms of no definite frequency	Often synchronous
8	H. J.	32	Anxiety neurosis	Gross twitches of no definite frequency	Often synchronous
9	W. M.	22	Operational fatigue	Diffuse with no definite frequency; no clear interspaces	Synchronous
10	S. W.	40	Mixed psychoneurosis	Diffuse tremor on extension only; at least 10 per sec., with no clear interspaces	No tremor in flexors
11	D. M.	21	Anxiety and depression	Irregular, 8-9 per sec.; no clear interspaces	No tremor in antagonists
12	W. H.	35	Depression with anxiety	Irregular, 8-10 per sec.; no clear interspaces	No tremor in antagonists
13	G. H.	24	Anxiety neurosis	Irregular, but approximately 10 per sec.	Often synchronous
14	R. C.	21	Post-traumatic anxiety neurosis with hysteria	8 per sec., with clear interspaces	Alternating from flexors to extensors
15	H. H.	37	Anxiety neurosis	Diffuse tremor on extension, not less than 9 per sec.; no clear interspaces	Sometimes synchronous
16	A. B.	19	Operational fatigue	Very fast, diffuse tremor; no definite frequency; no clear interspaces	Diffuse tremor in antagonists
17	R. R.	22	Anxiety neurosis	Very slow, 3 per sec., tremor on extension; no clear interspaces	Not present in flexors
18	R. M.	24	Anxiety neurosis	7-8 per sec. but very irregular; interspaces not very clear	Synchronous in antagonists
19	J. J.	42	Anxiety neurosis	Diffuse tremor with no clear interspaces; frequency approximately 10/12 per sec.	Present in extensors and flexors and sometimes exactly synchronous
20	W. A.	24	Anxiety neurosis	Diffuse tremor on volitional movement only; irregular with no clear interspaces; frequency varies from 7-11 per sec.	Present in opposing muscles but not exactly synchronous

Not only do these tremors fail to alternate from agonist to antagonist, but in some cases the discharges are truly synchronous in the opposing muscles; i. e., the individual spikes of muscle discharge occur exactly synchronously in antagonists (fig. 4, case 18).

Since in case 14 the electromyogram proved to have such consistently exceptional features, the symptoms and history will be given in rather more detail.

CASE 14.—R. C., a 21 year old seaman, forward gun captain, had served on three ships (transports and tankers). Eight months previous to the test he fell through an open hatch 35 feet (10.6 meters) to the deck below. He stated that "his back was broken" and that he lost consciousness. After several months in the hospital he was discharged as well, but one month prior to the test he first noticed disturbance of gait and onset of tremor. He also had insomnia, anorexia, nausea, vomiting, diarrhea and frequent headaches. His attitude toward his symptoms was expressed as follows: "All I need to get well is to have no one paying attention to me all the time. If these doctors would lay off. If people wouldn't try to help me. I try to walk straight."

His childhood history revealed finickiness toward food, rare nightmares and night talking but no sleepwalking. He had no history of enuresis, nail biting or spells of any kind.

On neurologic examination there were a pronounced tremor of the arms and considerable disturbance of gait. This was not the forward-leaning, propulsive type of gait common in patients with paralysis agitans but, rather, a lurching gait with buckling of the left knee. No rigidity or excessive salivation was noted.

This one exception to the pattern of the electromyogram in this series of cases of combat neurosis is found also to be the only case of tremor of post-traumatic origin. The obvious question arises as to whether this case may not be one of tremor of early paralysis agitans consequent to injury, and the patient's attitude toward his symptoms may contribute to this opinion.

The 3 cases among these service men in which the diagnosis was tremor of postencephalitic

paralysis agitans can be summarized briefly as follows:

L. C., a 31 year old seaman, presented the following symptoms: cogwheel rigidity of the arms and legs; tremor of the hands, arms and legs; spastic gait; dizzy spells with blurring of vision, and tremor, most marked in the legs, where it alternated from the anterior tibial to the gastrocnemius muscle. He had a history of diphtheria with delirium at the age of 8 years. The electromyogram showed a very regular tremor, of 6 per second frequency, of smooth pattern and with clear interspaces. The diagnosis was postencephalitic paralysis agitans.

P. G., a 34 year old seaman, had tremors of the hand, tongue, head and right leg, dating from an attack of influenza in 1918. The right side of his face was

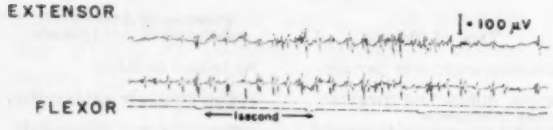

Fig. 4.—Tremor in a case of combat neurosis (case 18, table 1). Note the irregularity of the tremor and the synchrony of many of the discharges.

smoothed out. There was a pill-rolling movement of the thumb and finger of the right hand. There was no loss of associated movements or excessive salivation. The electromyogram showed a regular, 7 per second tremor of smooth pattern, alternating from flexor to extensor, with almost clear interspaces between the tremor bursts. The diagnosis was postencephalitic paralysis agitans.

K. M., a 36 year old seaman, had tremor of the right arm, diminution of associated movements in the right arm on walking and a slight stoop suggestive of rigidity of the neck characteristic of paralysis agitans. He had a history of pneumonia with delirium at 9 years of age, blood poisoning with delirium at 22, head injury with loss of consciousness at 33 and a second head injury with loss of consciousness at 35. The electromyogram showed a 6 per second tremor, alternating from flexor to extensor. The diagnosis was early paralysis agitans following multiple cerebral trauma (fig. 5).

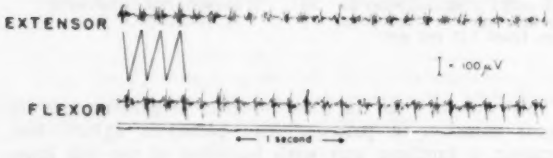

Fig. 5.—Tremor in a case of paralysis agitans (K. M., a 36 year old seaman). Note the regularity of rhythm, the 6 per second frequency and the alternation of tremor bursts from flexor to extensor muscle.

In this small series of cases occurring among service personnel, all of whom had seen combat, some differentiating characteristics have appeared in the electromyograms in 20 cases of combat neurosis as compared with the electromyograms in 3 cases of paralysis agitans. These differentiating features were in the main as follows:

1. The frequency of tremors seen in the combat neuroses is in general much faster and more diffuse than that of the tremor of paralysis agitans, and in cases in which the rhythm is well defined it is usually irregular in timing.

2. There is rarely a clear space between the tremor bursts, the potentials usually being diffuse, with some waxing and waning of the voltage, which coincides with the tremor movement.

3. The burst of potential accompanying the tremor movement does not have a smooth build-up to the maximum voltage followed by a smooth decline, such as is usually found in the tremor of paralysis agitans, but has a much more irregular pattern, of great variability.

4. In the cases of combat neurosis the tremor does not alternate from agonist to antagonist and is often even exactly synchronous in opposing muscles.

Since this series is small, it may be of interest to compare these records with the electromyograms in some civilian cases of paralysis agitans and of tremor of other origins.

In table 2 are summarized the observations in 10 cases of paralysis agitans from the wards and the outpatient department of the Massachusetts General Hospital.

It will be seen that an outstanding characteristic in all these cases is the regularity of the tremor. In every case the rhythm was well marked and of a frequency slower than is found in the cases of combat neurosis. In all these 10 cases the frequency was in the range of 4 to 7 cycles per second. In each of the 6 cases in which electromyographic data were obtained for antagonist muscles the tremor was found to alternate in opposing muscles. One of these (case 4) is illustrated in figure 1.

There are also data on 10 cases of civilian psychoneuroses, and these have been summarized in table 3. These cases were all from the psychiatric wards and the outpatient department of the Massachusetts General Hospital. In these cases the tremors were in general much less gross than in the cases of combat neurosis, with the single exception of case 6, which is illustrated in figure 6.

Here, as in the cases of combat neurosis, the tremors were fast in frequency, diffuse in pattern and irregular in timing. Irregularity of rhythm in hysterical tremors was described and demonstrated electromyographically by Cobb, in 1920.[5]

5. Cobb, S.: Electromyographic Studies of Muscles During Hysterical Contraction, Arch. Neurol. & Psychiat. **4**:8-15 (July) 1920.

In no case in the present series did the tremor alternate from agonist to antagonist. In some cases the exact synchrony of discharges in opposing muscles was striking, as, for example, in case 6 of table 3. This is the case illustrated in figure 6.

Another type of tremor on which some electromyographic data are available is the alcoholic tremor. An example of such a tremor in the case of a patient admitted in delirium tremens is shown in figure 7. In this case the tremor is rather slower than most tremors of paralysis agitans (4 per second) and is fairly regular in pattern but is markedly synchronous in extensor and flexor groups.

There is another differentiating characteristic of these tremors which has not been dealt with here, since it is easily detectable with the naked eye and one does not need the help of an electromyogram to determine it. This is the observation that the tremor of paralysis agitans is usually more intense in the resting state and tends to decrease with the patient's attempt at a fine movement, whereas the reverse is true with the tremor of psychoneurosis; the latter usually becomes far more severe with intention.

TABLE 2.—*Electromyographic Data on Tremors of Paralysis Agitans*

Case No.	Patient	Age	Diagnosis	Type of Tremor	Alternation in Antagonists
1	H. R.	48	Postencephalitic paralysis agitans	Regular, 5 per sec. tremor of right arm with clear interspaces	Alternation from extensor to flexor
2	H. B.	25	Post-traumatic paralysis agitans	Regular, 5 per sec. tremor of left arm; clear interspaces	Alternation from extensor to flexor
3	M. F.	23	Postanoxic paralysis agitans	Regular, 5-6 per sec.	No data
4	A. P.	61	Arteriosclerotic paralysis agitans	Regular, 6 per sec.	Alternation from gastrocnemius to anterior tibial muscle
5	E. B.	35	Postencephalitic paralysis agitans	Very regular, 5 per sec.	No data
6	J. C.	35	Post-traumatic paralysis agitans	Regular, 5 per sec.; clear interspaces	Alternation from flexor to extensor
7	F. E.	68	Arteriosclerotic paralysis agitans	Regular, 5 per sec.	No data
8	A. T.	54	Right-sided paralysis agitans	Regular, 4 per sec.; clear interspaces	No data
9	F. S.	28	Congenital dysfunction of extrapyramidal system	7 per sec., irregular in pattern	Alternation in antagonists
10	J. J.	71	Paralysis agitans	Regular, 4 per sec. tremor	Alternation in antagonists

TABLE 3.—*Electromyographic Data on Tremors in Civilian Cases of Psychoneuroses*

Case No.	Patient	Age	Diagnosis	Type of Tremor	Alternation in Antagonists
1	C. S.	31	Mixed psychoneurosis with hypochondriasis	Diffuse, irregular tremor in arm; some rhythm at 11-13 per sec.	None
2	M. G.	33	Anxiety neurosis with depression	Diffuse; some rhythm at 11 per sec.	None
3	K. G.	38	Hysteria with anxiety	Irregular, with variable frequency; never less than 12 per sec.	Often synchronous in extensor and flexor
4	M. S.	27	Conversion hysteria	Very diffuse; some rhythm at 7 per sec.	Some synchrony between extensor and flexor
5	V. M.	18	Hysteria	5-6 per sec.; irregular pattern	Synchronous in extensor and flexor
6	C. B.	21	Hysteria with psychopathic behavior	Extremely irregular, rhythm varying from 3-15 per sec.	Always exactly synchronous in opposing muscles
7	O. R.	26	Mixed psychoneurosis with hysteria and hypochondriasis	Very diffuse, with no defined pattern	Continuous in opposing muscles
8	G. G.	26	Anxiety neurosis	Bursts of potentials of approximately 2 per sec.	Synchronous in flexor and extensor
9	E. D.	21	Hysteria	Diffuse, with no definite rhythm	Continuous in opposing muscles with some synchronous spikes
10	D. H	27	Hysteria	Diffuse, with some irregular rhythm, from 10-12 per sec.	Often synchronous in opposing muscles

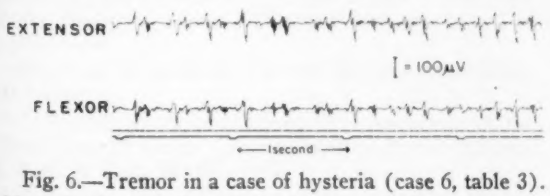

Fig. 6.—Tremor in a case of hysteria (case 6, table 3). Note the irregularity of the bursts and the exact synchrony between the individual discharges in extensor and flexor muscles.

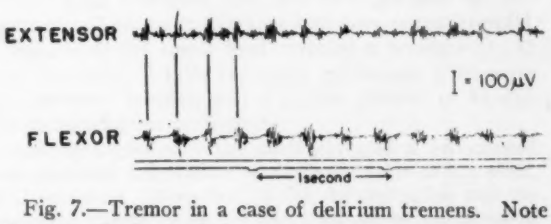

Fig. 7.—Tremor in a case of delirium tremens. Note the slow rhythm and the synchrony of tremor bursts in opposing muscles.

The tremor of paralysis agitans is thought to be due to loss of controlling impulses from the extrapyramidal system which integrate involuntary movement patterns, locomotion and the stabilization of posture.[6] The primitive type of innervation pattern which impairment of these regulating mechanisms releases results in a fairly consistent electromyographic picture in the muscles involved. But the mechanism by which the tremor is caused is still far from clear. There is, for example, the observation of Wechsler [7] that the tremor of paralysis agitans can be abolished by obliterating the arterial pulse by a tourniquet on the limb; there are the various attempts to abolish the tremor by partial section of the motor tracts of the spinal cord (Putnam [8]), by section of the precentral cortex (Bucy and Case [9] and Klemme [10]) and by section of the ansa (Meyers [11]).

Whatever the mechanism of the tremor of paralysis agitans, it is clear that a very different one is concerned with the tremor of psychoneurosis. The electromyographic pattern is quite different and may give leads for further elucidation of the pathways involved. One feature of the electromyogram is the diffuse nature of the potentials in many cases; in this respect they are similar to action potentials of cortical origin. It would be interesting to check this more closely by the use of needle electrodes in the muscle. Another, and perhaps the most outstanding, feature is the absence of alternation in opposing muscles. The alternate innervation of opposing muscles in paralysis agitans has some similarity to clonus, which is a reflex mechanism in the cord. This clonic type of activity is not seen in the tremors of psychoneurosis.

6. Benda, C. E., and Cobb, S.: On the Pathogenesis of Paralysis Agitans, Medicine **21**:95-142, 1942. Fulton, J. F.: Physiology of the Nervous System, New York, Oxford University Press, 1943. Tower, S. S.: Extrapyramidal Action from the Cat's Cerebral Cortex: Motor and Inhibitory, Brain **59**:408-444, 1936.

7. Wechsler, I. S., in discussion on Pollock, L. J., and Davis, L.: Muscle Tone in Parkinsonian States, Arch. Neurol. & Psychiat. **23**:303-319 (Feb.) 1930.

8. Putnam, T. J.: Operative Treatment of Diseases Characterized by Involuntary Movements (Tremor, Athetosis), A. Research Nerv. & Ment. Dis., Proc. (1940) **21**:666-696, 1942.

9. Bucy, P. C., and Case, T. J.: Athetosis: Surgical Treatment of Unilateral Athetosis, Arch. Neurol. & Psychiat. **37**:983-1020 (May) 1937.

10. Klemme, R. H.: Surgical Treatment of Dystonia, A. Research Nerv. & Ment. Dis., Proc. (1940) **21**:596-601, 1942.

11. Meyers, R.: Modification of Alternating Tremors, Rigidity and Festination by Surgery of Basal Ganglia, A. Research Nerv. & Ment. Dis., Proc. (1940) **21**:602-665, 1942.

SUMMARY

Electromyographic studies were made on the tremors of 23 men of combat personnel. Of these patients, 3 had symptoms of lesions of the extrapyramidal tract, and 20 had a condition diagnosed as combat neurosis.

In addition, studies were made on 10 civilians with paralysis agitans and 10 civilians with tremors associated with psychoneurosis.

Electromyographic data are given on tremor in a case of delirium tremens.

The following electromyographic differences were found between the tremor of paralysis agitans and tremors of psychoneurotic origin:

1. The rate of tremors associated with psychoneurosis is usually faster than that of tremors of paralysis agitans and is often so fast as to give a completely diffuse electromyogram, with no discernible rhythm.

2. The tremor of psychoneurosis does not have the clearly patterned discharge of smooth increase in the voltage to a maximum followed by a smooth decrease that is typical of tremor of paralysis agitans.

3. Clear interspaces between the individual tremor bursts are rarely found in cases of psychoneurosis.

4. Tremor bursts associated with psychoneurosis do not alternate from agonist to antagonist as in paralysis agitans but usually appear simultaneously in opposing muscles, and sometimes are even exactly synchronous in the timing of the individual discharge.

Comdr. J. M. Henninger (MC), U.S.N.R., continued to make available the facilities for this work after Lieut. Comdr. H. I. Harris had gone overseas, and Miss Margaret Gray gave technical assistance in recording the tremors.

Massachusetts General Hospital.

ARTERIOVENOUS ANEURYSM OF GREAT CEREBRAL VEIN AND ARTERIES OF CIRCLE OF WILLIS

FORMATION BY JUNCTION OF THE GREAT CEREBRAL VEIN AND THE STRAIGHT SINUS AND BY THE CHOROIDAL ARTERIES AND ANOMALOUS BRANCHES OF THE POSTERIOR CEREBRAL ARTERIES

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Arteriovenous aneurysm of the great cerebral vein (Galen) and the arteries of the circle of Willis is so rare that it seems desirable to record an instance of the condition. Only 2 other cases heve been recorded in the literature [1] and a third [2] is unquestionably a typical example of the disorder.

REPORT OF A CASE

History.—R. L. V., an 18 year old youth, entered the Jefferson Hospital on May 9, 1944 and died on June 16, 1944. He had had headaches since he was 6 years old and had suffered from them intermittently until his death. They were largely frontal in location, and they occurred at an average frequency of one or two a week. His headaches were at first relieved by acetylsalicylic acid and were not so severe as to interfere with his activities. Two months before entrance into the hospital, however, they became more severe, and they then lasted most of the day. In the last month the headaches were accompanied with dizziness, characterized by the movement of objects in the environment. Beyond this there was nothing significant in the patient's story and nothing of importance in the past history.

Neurologic Examination.—The patient was somewhat euphoric, highly distractible and rather flippant. His reactions were slow, and his intelligence appeared subnormal. The pupils were equal and regular and reacted promptly to light, in accommodation and to consensual stimuli. The optic nerves were well defined and had good color, and the retinas appeared healthy. The visual fields were full as determined by perimetric test, and visual acuity was 20/20 in each eye. The blindspots were not enlarged. Ocular movements were good in all directions. The corneal reflexes were active. There was no facial weakness. Tuning fork tests revealed normal hearing. There was no weakness of the palate or tongue. There was good power in all the limbs except in the right hand, in which the grip seemed slightly weaker than that in the left. The heel-knee test was performed accurately but with a coarse tremor; the patient tended to lose his balance in standing on either foot alone, and there was a little difficulty in performing the heel-toe test. There was no dyssynergia of the limbs or trunk. The gait was steady. The biceps, triceps, radial, achilles and patellar reflexes were active and equal on the two sides. There were no pathologic reflexes. The abdominal reflexes were active. Sensory examination gave normal results for all modalities.

Laboratory Studies.—The mental age was 9 and 8/12 years and the intelligence quotient 64 by the Stanford-Binet test. A similar examination seven years previously revealed an intelligence quotient of 73.

Electroencephalographic studies revealed no evidence of a focal lesion and no indication of abnormal brain waves.

Studies of the blood revealed 4,200,000 red cells, 4,100 white cells and a hemoglobin concentration of 75 per cent. The Wassermann reaction of the blood was negative. The urea was 9.2 mg. and the blood sugar 71 mg., per hundred cubic centimeters.

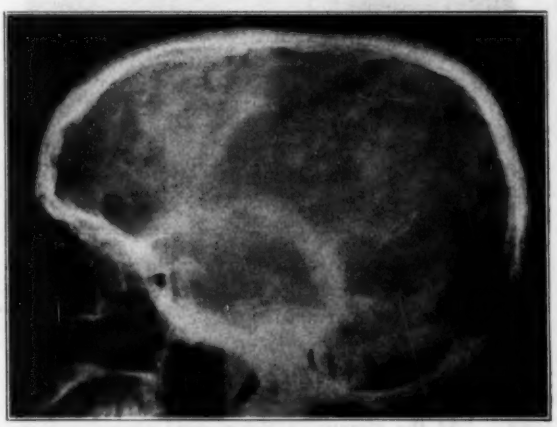

Fig. 1.—Lateral view of the skull, showing the evidence of increased pressure on the inner table of the skull and the crescentic calcified shadow in the posterior portion of the skull.

Urinalysis on five occasions revealed a specific gravity of 1.012 to 1.020, without casts, blood, albumin or sugar. Urea clearance was 50 per cent.

The basal metabolic rate was +4 per cent on one occasion. The sugar tolerance test gave normal results.

Studies of the spinal fluid revealed a pressure of 185 mm. of water, 2 cells per cubic millimeter, a negative Wassermann reaction and a protein content of 51 mg. per hundred cubic centimeters.

Roentgenograms of the skull revealed a pronounced convolutional indentation of the inner table of the skull, with complete destruction of the dorsum sellae and the posterior clinoid processes and apparent enlargement of

From the Department of Neurology, Jefferson Medical College.

1. Russell, D. S., and Nevin, S.: Aneurysm of the Great Vein of Galen Causing Internal Hydrocephalus, J. Path. & Bact. **51**:375, 1940.

2. Jaeger, R.: Personal communication to the authors.

the sella turcica. In the right parieto-occipital region was a crescentic rim of calcification, above which lay irregularly mottled calcified areas.

Course.—Because of the history of persistent headache and the evidence of calcification in the roentgenogram, a diagnosis of brain tumor was made in spite of the normal pressure. The latter failed to correspond to the indications of pressure shown in the roentgenogram. Since there were no indications of a localized lesion except for the calcified shadow in the roentgenogram and the inconclusive evidences of incoordination on neurologic examination, pneumoencephalographic examination was deemed advisable. An encephalographic study was made but was not successful in revealing the location of the lesion.

Ventriculographic examination, performed by Dr. Rudolph Jaeger, revealed greatly dilated ventricles. The calcified mass appeared to project into the posterior horn of the right lateral ventricle.

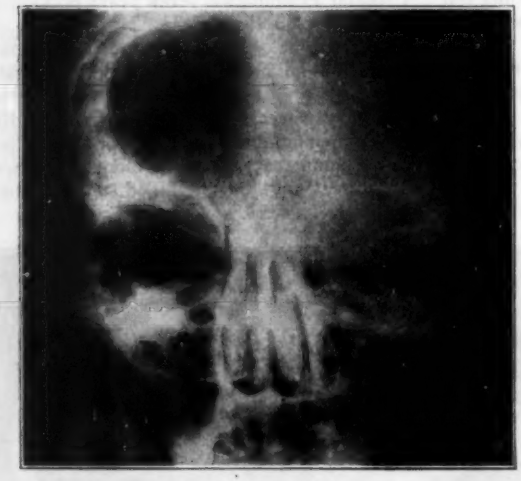

Fig. 2.—Ventriculogram, showing filling of one ventricle only, with a calcified shadow appearing on the mesial aspect of the ventricle.

Craniotomy (Dr. Rudolph Jaeger).—The right lateral ventricle was opened. The report of the operation follows: "At the glomus of the choroid plexus a large, tortuous mass of arteries and veins was found. These ran toward the base of the skull and connected with the large vessels, supplying an aneurysm about the size of a hen's egg. It was necessary to cut through the floor of the lateral ventricle in order to expose the mass. It lay tightly against the tentorium with its vascular stem of attachment toward the midline. It was apparently an aneurysm of a branch of the circle of Willis, probably the posterior cerebral artery. A part of its wall was calcified, and it had a strong pulsation."

The patient reacted poorly to the operation and died two days after the craniotomy. Necropsy was performed.

Gross Description of Brain.—The cerebral hemispheres revealed nothing of significance except a severe degree of internal hydrocephalus, involving all parts of the lateral ventricles. The third ventricle was enlarged. The aqueduct of Sylvius was not dilated, and the fourth ventricle was normal in size. The shape and configuration of the cerebral hemispheres were not unusual, and the cerebral vessels and the meninges over them were normal.

The brain was sectioned horizontally, since it was apparent from the approach through the operative field that a large aneurysm was present. This lay between the cerebral hemispheres. The brain mantle was cut away serially in horizontal sections in order to disclose the aneurysm clearly. After study of its relationships as it lay exposed, it was dissected away carefully in order to disclose its features at lower levels. Photographs and drawings were made at each level before each step in dissection.

The aneurysm lay between the cerebral hemispheres, occupying the pineal recess and resting on the tectum mesencephali. It measured 4 by 2.5 by 2.5 cm. It was dome shaped, its broadest portion lying superiorly, with a narrow waist at the point of its union with the vessels of origin. The walls were firm and dense but measured only 2.5 to 3 mm. in thickness. Dissection revealed that the body of the aneurysm arose from the junction of the great cerebral vein (Galen) with the straight sinus, but it was not possible to determine which of the two vessels contributed most to its formation. The probabilities are that the great cerebral vein was most involved, since it was greatly dilated for 1 inch (2.5 cm.) before the aneurysmal sac was reached. Nothing could be determined concerning the other dural sinuses, since these were not dissected out at the time of removal of the specimen.

The point of greatest interest lay in the connection of the aneurysm with the arteries of the circle of Willis. As the aneurysm lay exposed, rich arterial supplies could be followed into it from both choroidal arteries, which lay in a maze of smaller arteries and veins on the floor of each lateral ventricle. Direct communication could be established between the aneurysm and the choroidal arteries. These, in turn, could be traced to communications with the posterior cerebral artery on each side.

The circle of Willis revealed normal anterior cerebral, anterior communicating, vertebral and basilar arteries. The basilar artery divided normally into the two posterior cerebral arteries, but a branch from each posterior cerebral vessel could be followed coursing around the mesencephalon, sending branches into the aneurysm. On the tectum of the midbrain lay a maze of vessels connected with the posterior cerebral arteries, sending many branches into the wall of the aneurysm. From the left middle cerebral artery came an aberrant branch, which was connected with the basilar artery by aberrant vessels enclosing the oculomotor nerve. There were several aberrant branches from the posterior cerebral arteries.

Microscopic examination of the great cerebral vein revealed a hyperplastic intima and a thickened adventitia. The wall of the aneurysm revealed a thickened and hyperplastic intima and an adventitia of abundant, loose connective tissue. There was no evidence of infiltration in the walls of either the vein or its aneurysm.

COMMENT

Only 2 previous cases of aneurysm of the great cerebral vein have been recorded (Russell and Nevin [1]). The 2 cases reported by Russell and Nevin concerned infants of 17 months. In their

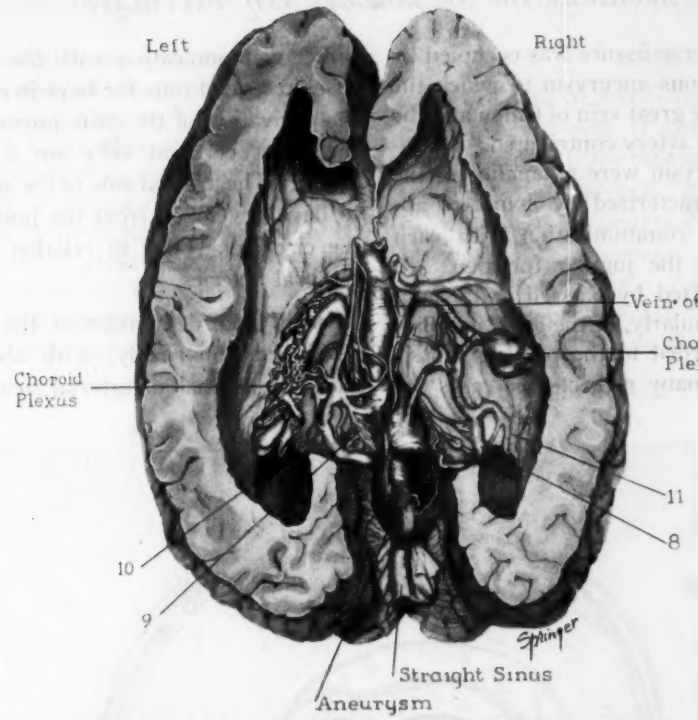

Fig. 3.—Horizontal section of the brain, showing the position of the aneurysm, the great cerebral vein (Galen) and the straight sinus, as well as the arterial supply. In this figure, and in figure 2, the arteries are designated as follows: (*1*) basilar, (*2*) left posterior cerebral, (*3*) left posterior communicating, (*4*) aberrant artery on left, (*5*) right posterior communicating, (*6*) right posterior cerebral, (*7*) aberrant artery on right, (*8*) aberrant artery on right choroidal artery and to aneurysm, (*9*) and (*10*) aberrant artery on left and (*11*) right posterior choroidal.

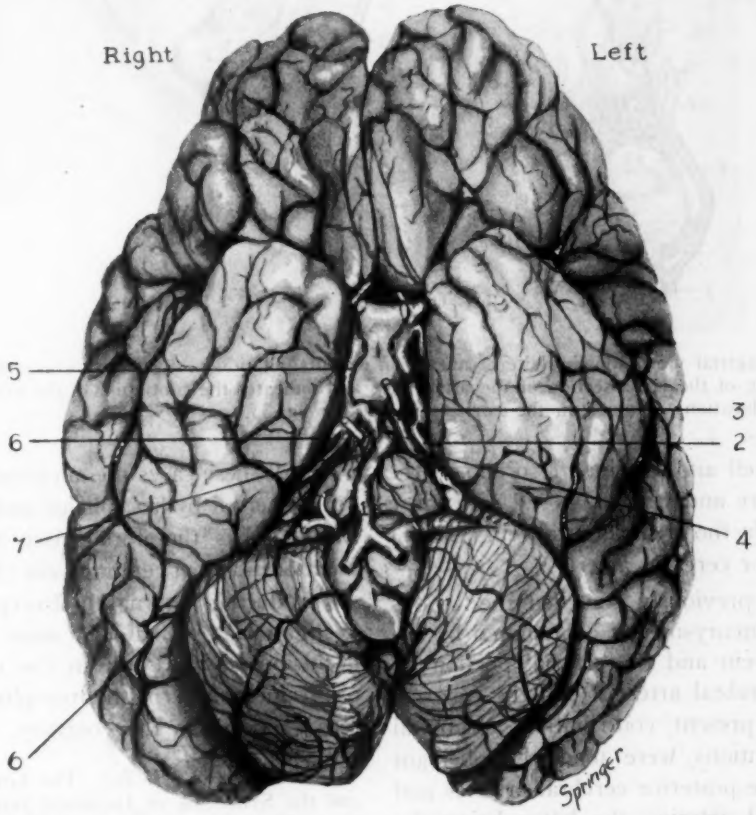

Fig. 4.—View of the base of the brain, demonstrating the anomalies of the circle of Willis and the derivation of the arteries supplying the aneurysm.

first case "the transverse fissure was occupied by a complex arteriovenous aneurysm to which the torcular Herophili, the great vein of Galen and the left posterior cerebral artery contributed." Associated with the aneurysm were anomalies of the venous channels characterized by complete absence of the venous communication with each jugular vein through the jugular foramen. In the second case reported by Russell and Nevin the aneurysm was, similarly, of the great cerebral vein. The case recorded in the present contribution resembles in many respects the cases reported by Russell and Nevin. It occupied the transverse fissure and was composed of a large sac contributed by the great cerebral vein (Galen) and the posterior cerebral arteries.

In the cases previously recorded the venous portion of the aneurysm was contributed by the great cerebral vein and the arterial portion by the posterior cerebral arteries. In the case recorded in the present contribution additional arterial contributions were made by aberrant arteries from the posterior cerebral arteries and by the choroidal arteries, the latter being the direct communication with the aneurysm. The cases recorded thus far have in common not only the derivation of the main aneurysmal wall from the great cerebral vein but a similar arterial origin. The arterial side of the aneurysm appears to have developed from the posterior portion of the circle of Willis in relation to the posterior cerebral arteries.

In all recorded instances the circle of Willis developed abnormally, with aberrant branches and with anomalous arterial stems.

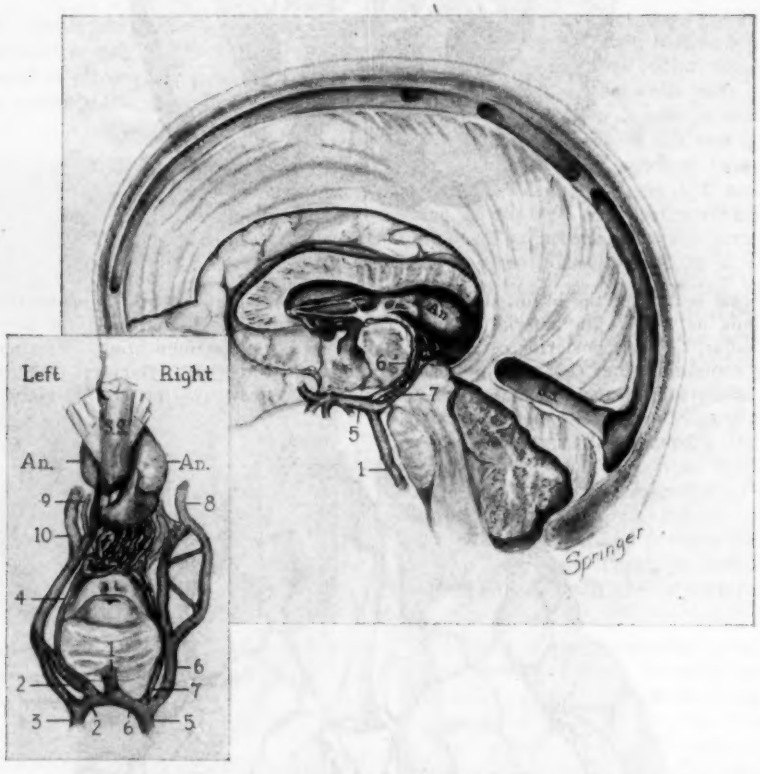

Fig. 5.—Parasagittal view, showing site of aneurysm and its relation to the falx, sinuses and ventricles. The insert is a drawing of the cross section of the brain stem and indicates the continuity of the vessels from the circle of Willis to the locations obtained in the horizontal section (fig. 3).

In all these cases the aneurysm was associated with internal hydrocephalus and headache. The problem has therefore arisen whether involvement of the great cerebral vein (Galen) is capable of producing internal hydrocephalus. The investigations of Bedford [3] seem to indicate that occlusion of this vein in the dog is incapable of producing internal hydrocephalus, despite scattered reports to the contrary. It seems more

3. Bedford, T. H. B.: The Great Vein of Galen and the Syndrome of Increased Intracranial Pressure, Brain **57**:1, 1934.

probable, therefore, that the hydrocephalus found in the recorded cases of aneurysm of the great cerebral vein was not the result of involvement of this vein itself but, rather, the effect of pressure on and occlusion of the aqueduct of Sylvius, though this is by no means definite. The cause of the associated hydrocephalus is not clear, but it remains a matter of great clinical interest that in all the recorded cases (Russell and Nevin; Jaeger; Alpers and Forster) the aneurysm has been associated with internal hydrocephalus.

SUMMARY

In the case of arteriovenous aneurysm of the great cerebral vein (Galen) recorded here, the venous side of the aneurysm was formed by the great cerebral vein, and the arterial supply came through the posterior cerebral and choroidal arteries. The aneurysm appears to have been congenital in origin. As in the 2 previously recorded cases, internal hydrocephalus was the only clinical feature of significance.

INCIDENCE OF ADVANCED MATERNAL AGE IN MOTHERS OF ONE THOUSAND STATE HOSPITAL PATIENTS

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Advanced maternal age has been shown to be related to a number of pathologic conditions in the offspring. While considerable attention has been devoted to a study of maternal age as related to such conditions as achondroplasia,[1] congenital cranial osteoporosis,[2] multiple births,[3] monstrosities[4] and abnormally large fetuses,[5] the maternal age at birth of children who subsequently become psychotic has received little emphasis. Gordon[6] reported 30 cases. His conclusion that "late marriage seems to favor the development of mental disorders in the offspring" seems rather sweeping on the basis of such a small series. Kawin[7] made the statement that parents of problem children tend to be slightly older than average. In general, however, the age of mothers at the time of birth of children who subsequently become psychotic has been almost universally ignored.

Several conditions involving the central nervous system have been shown to be related to maternal age. Of these, mongolism appears to have been investigated most thoroughly. Marston[8] showed in 1925 that 37 per cent of the mothers of mongolian idiots were 40 years of age or over at the birth of their defective offspring, as compared with 2.1 per cent of mothers over 40 in a control series. Since then, numerous investigators have confirmed and amplified his findings which relate mongolism to advanced maternal age, including Bleyer[9] and Penrose.[10] However, Rosanoff and Handy[11] and others emphasized the fact that young mothers may give birth to offspring with mongolism, and Southwick[12] has shown that births of mongolian idiots are not infrequently followed by the birth of a normal sibling. It is evident that advanced maternal age is in some manner related to mongolism, although other factors are more immediately involved in the pathogenesis of this condition.

METHOD AND DATA

The present investigation is concerned with the age distribution of mothers at the time they gave birth to children who subsequently became psychotic. A series of 1,000 case histories were studied, for which the necessary data were available. The patients[13] were white persons representing first admissions to the New Jersey State Hospital, at Greystone Park, N. J., who were over 15 and under 40 years of age at the time of their admission to the hospital during the period 1930 to 1938. Patients over 40 were not included because of the relative paucity of information which is obtainable for older patients.[14] Data were secured from anamneses obtained by the social service department. These anamneses form part of the clinical record of the patients and are based on interviews with members of the patient's family, confirmed by other investigation when indicated. Anamneses at this hospital are complete and were obtained

From the Department of Neurology and Psychiatry of the Harvard Medical School, and the Department of Psychiatry of the Massachusetts General Hospital.

1. Bleyer, A.: Role of Advancing Maternal Age in Causing Achondroplasia, Am. J. Dis. Child. **58**:994-1000 (Nov.) 1939.
2. Reiss, O., and Boder, E.: Congenital Cranial Osteoporosis, Am. J. Dis. Child. **59**:931-1001 (May) 1940.
3. Guttmacher, A. F.: Analysis of 521 Cases of Twin Pregnancy, Am. J. Obst. & Gynec. **34**:76-84, 1937.
4. Murphy, D. P.: Congenital Malformations, Philadelphia, University of Pennsylvania Press, 1940.
5. Curtis, A. H.: Obstetrics and Gynecology, Philadelphia, W. B. Saunders Company, 1933, vol. 2.
6. Gordon, A.: Incidence of Psychotic Disorders in Individuals Whose Parents Married at an Advanced Age, M. Rec. **148**:109-112, 1938.
7. Kawin, E.: Children of Pre-School Age, Chicago, University of Chicago Press, 1934.
8. Marston, L. R.: Etiology of Mongolism, Psychol. Clin. **16**:135-140, 1925.
9. Bleyer, A.: Role of Advancing Maternal Age in Mongolism: A Study of 2,822 Cases, Proc. Am. A. Ment. Deficiency **61**:111-123, 1937.
10. Penrose, L. S.: Maternal Age, Order of Birth, and Developmental Anomalies, J. Ment. Sc. **85**:1141-1150, 1939.
11. Rosanoff, A. J., and Handy, L. M.: Etiology of Mongolism with Special Reference to Its Occurrence in Twins, Am. J. Dis. Child. **48**:764-779 (Oct.) 1934.
12. Southwick, W. E.: Time and Stage in Development at Which Factors Operate to Produce Mongolism, Am. J. Dis. Child. **57**:68-89 (Jan.) 1939.
13. Dr. Marcus A. Curry made the case histories available.
14. Barry, H., Jr., and Bousfield, W. A.: Incidence of Orphanhood Among Fifteen Hundred Psychotic Patients, J. Genet. Psychol. **50**:198-202, 1937.

by several different social workers, none of whom knew that the present investigation was contemplated. The results are presented in figure 1, which shows the distribution of maternal ages at the time of birth of these mental hospital patients. Maternal ages according to figures of

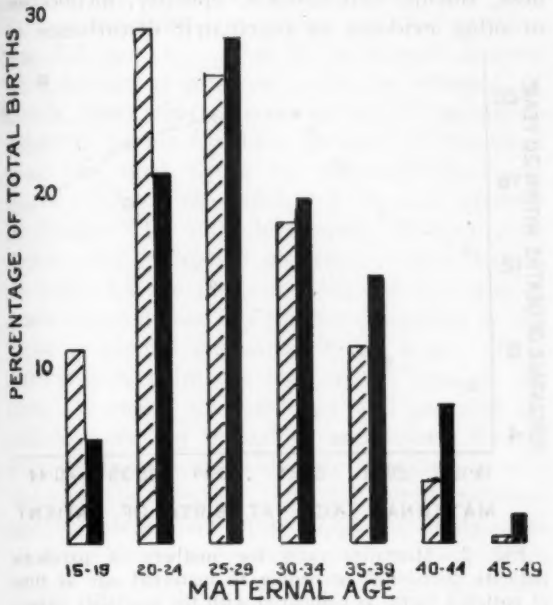

Fig. 1.—Percentage of births of normal and of psychotic persons plotted against the maternal age at birth. The solid rectangles represent psychotic patients; the cross-hatched rectangles, normal persons.

the United States Bureau of the Census, which include 7,000,000 births,[15] are presented as a control. The bar diagram indicates that the mothers of 1,000 state hospital patients are

TABLE 1.—*Ages of Mothers at Birth for Series of 1,000 Patients*

Age of Mother	Number of Patients		
	Male	Female	Total
16-19	37	24	61
20-24	113	99	211
25-29	149	137	286
30-34	91	104	195
35-39	67	86	153
40-44	35	44	79
45	9	6	15
Total	500	500	1,000
No information	270	212	482

slightly, but quite consistently, older than the average. The differences are most apparent at the extremes: that is, for the oldest and youngest mothers. Table 1 gives data for maternal ages subdivided according to the sex of the patients. It will be noted that female patients in general show a slight tendency to have older mothers than male patients; in other words, the "shift to the right" in maternal age, which was noted for psychotic patients in figure 1, is accentuated in the case of females.

Although the number of patients for whom information on maternal age is lacking is large, there is no reason to suppose that the maternal ages for these patients would be materially lower than one for patients for whom data are available.

In table 2, the series is subdivided according to the clinical diagnosis. It will be seen that most of the subgroups are small, so that percentage differences would have little significance;

TABLE 2.—*Diagnoses for a Series of 1,000 Patients in a State Hospital*

Diagnosis	Number of Patients			Patients with Mother Over 40 at Birth of Patient	
	Male	Female	Total	No.	Per Cent
Dementia precox	348	236	584	53	9
Manic-depressive psychosis	37	135	172	18	11
Psychoses with mental deficiency	23	27	50	7	*
Psychopathic personality	20	19	39	1	*
Syphilis of central nervous system	20	5	25	1	*
Psychoneurosis	3	18	21	3	*
Epilepsy	11	11	22	4	*
Epidemic encephalitis	13	5	18	3	*
Undiagnosed condition	8	10	18	4	*
Paranoid condition	3	9	12	0	*
Alcoholic psychosis	9	0	9	0	*
Postpartum psychosis	0	5	5	0	*
All other psychoses	5	20	25	0	*
Total	500	500	1,000	94	

* Number of patients in subgroups is so small as to make percentage comparisons unreliable.

these differences have, therefore, not been computed except for the larger groups. Even with manic-depressive psychoses a difference of 2 cases could decrease the percentage of mothers over 40 from 11 to 9 per cent. The series includes few patients whose psychosis was diagnosed as paranoid or alcoholic, owing to the preponderance of younger patients in this series.

As a further basis for comparison, the data for a group of psychoneurotic patients from the psychiatric outpatient department of the Massachusetts General Hospital were analyzed in the same way. Data were obtained for 222 patients, aged 12 to 25, whose disorders had been diagnosed as psychoneuroses or as behavior problems. Of this group, only 8, or 3.6 per cent, had mothers who were over 40 at the time the patient was born. This percentage is substantially lower than the comparable figure of 9.4 per cent for psychotic patients; it is approximately the same as the figure of 3.9 per cent for the population of the United States. While

15. Cited by Bleyer.[1]

findings based on 200 cases are at most suggestive, these figures do not indicate that maternal ages are increased for psychoneurotic patients.

A similar incidence was obtained for another group of psychoneurotic patients at the Riggs Foundation, Stockbridge, Mass. Data were made available through the courtesy of Dr. C. N. Kimberly. Out of 73 patients, only 3 had mothers who were 40 or over at the time the patients were born. Although the patients in this series represent, for the most part, a superior socioeconomic status, maternal ages were comparable to figures for normal persons or to those for psychoneurotic patients studied at the Massachusetts General Hospital. Because the series is not large, percentages have not been computed.

TABLE 3.—*Mortality Rates for Mothers of Psychotic Patients According to Maternal Age at Birth of Patient*

Age of Mother When Patient Was Born	Number of Patients: Mother Died When Patient Was Aged 0-19	20+	Mother Living	Total Number of Patients	Per Cent of Maternal Deaths, Patient 0-19 Yr. Old
15-19	8	7	46	61	13.1
20-24	31	18	162	211	14.7
24-29	56	30	200	286	19.6
30-34	38	19	138	195	19.5
35-39	28	30	95	153	18.3
40+	15	22	57	94	15.9
Not stated	128		259	382	Not stated
No data as to whether mother living or dead				100	

Table 3 indicates the mortality rates for mothers of psychotic patients, subdivided according to maternal age at the time of the patient's birth. Only 15.6 per cent of the mothers over 40 had died within twenty years, as compared with an expected mortality rate of 21.3 per cent. However, 13.1 per cent of the mothers under 20 died within twenty years, although the expected mortality was only 6.4 per cent.

The relationships which have been presented in table 3 are reproduced graphically in figure 2, which furnishes a comparison of actual and expected deaths among mothers of psychotic patients. Data for mortality expectation, by age groups, are computed on the basis of the life tables for white males and white females in the United States, 1929 to 1931.[15a]

Although the purpose of this paper is to indicate the age distribution of mothers of psychotic patients, the discussion would hardly be complete without some mention of heredity. One of the difficulties in evaluating the influence of heredity in mental disease is the establishment of satisfactory criteria as to what constitutes psychiatric abnormality in a parent. Since this paper is not concerned with the problem of heredity per se, any patient for whom there is a history of nervousness, irritability, mental illness, suicide, drunkenness, epilepsy, alcoholism or other evidence of psychiatric disturbance in either or both parents is taken to have a positive family history. While this criterion is admittedly indefinite and lacking in precision as a measure of genetic psychiatric abnormality, and though it includes only disorders reported for parents of patients, it may be useful as a relative measure of parental abnormality in patients with elderly and young mothers, respectively. The results are presented in table 4.

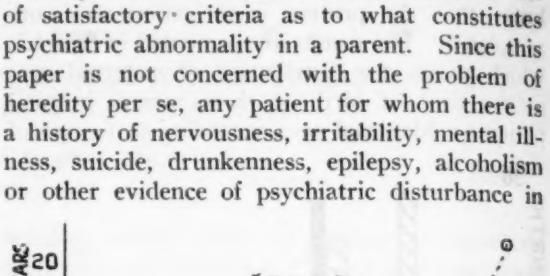

Fig. 2.—Mortality rates for mothers of psychotic patients distributed according to maternal age at time of patient's birth, as compared with the mortality expectation computed on the basis of the figures of the United States Bureau of the Census.[15]

TABLE 4.—*Incidence of Nervous Instability in Parents of Psychotic Patients*

Age of Mother at Birth of Patient	Cases of Parental Instability Reported	Cases in Which No Parental Instability Was Reported	Per Cent of Parental Instability
15-19	21	40	34.4
20-24	64	149	30.0
25-29	85	199	29.9
30-34	52	143	26.6
35-39	36	117	23.5
40+	24	70	25.5
Total	282	718	28.2

It is evident that if the relatives of psychotic patients who are considered for heredity were to include grandparents, nieces and cousins, the percentages of patients with a positive "heredity" would be materially higher than the figure just cited. On the other hand, if more rigorous

15a. Dublin, L. I., and Lotka, A. J.: Length of Life: A Study of the Life Table, New York, The Ronald Press Co., 1936, pp. 14-17.

criteria are employed, and the observations are limited to mothers alone, the percentages will be relatively small. For the patients of this series, 3.6 per cent of 1,000 mothers for whom parental ages were available and 9 per cent of 419 mothers for whom parental ages were unobtainable had a clearcut history of psychosis. The average incidence of psychoses for 1,419 mothers was 5.2 per cent. For 62 additional mothers no information whatever could be obtained; it seems likely that the percentage of psychoses would be higher for these persons. If this were true, the final figure for maternal psychoses might approach the value of 9 per cent reported by Bleuler [16] for 100 schizophrenic patients. Evidently, any evaluation of heredity must depend so much on the methods used and the type of cases selected that any further discussion of the topic is beyond the scope of this paper. It is sufficient to point out that on the basis of the data presented, maternal age and parental instability are not related to each other, though each of these factors evidently is related to psychoses in the offspring. In other words, maternal age is independent of parental instability, just as it was found to be independent of early death of the mother, for this group of psychotic patients.

Since there is evidence that maternal age and bereavement are independent variables and that maternal age and parental instability are also independent of each other, the relationship between bereavement and parental instability becomes of interest. Of 282 patients for whom parental instability is reported, 49, or 17.4 per cent, experienced the death of their mothers by the age of 19 years. Of 718 patients without report of parental instability, 131, or 18.2 per cent, experienced the death of their mothers by 19 years of age. While it seems doubtful that the maternal mortality rate would be higher for those without parental instability, and while a more probable explanation is that parental instability is less likely to be reported when the mother has been dead for some time, the figures are of interest. They indicate that for this series of 1,000 patients there are three groups of parental situations reported, with relatively little overlap: parental instability, 28.2 per cent; maternal bereavement, 17 per cent, and advanced maternal age, 9.4 per cent. All told, these three categories include 469 patients, or 46.9 per cent, of the entire series of patients for whom detailed information is available.

16. Bleuler, J.: A Contribution to the Problem of Heredity Among Schizophrenics, J. Nerv. & Ment. Dis. **74**:393-467, 1931.

COMMENT

Three points stand out as a result of this investigation. First is the large number of patients (94, or 9.4 per cent) whose mothers were over 40 years of age when the patients were born. Second is the large number of patients (174, or 17.4 per cent) whose mothers died before the patients were 20 years of age. Third is the paradoxic finding that the death rate was relatively higher for the younger mothers than for the older ones. Since the overlap between the first two categories is small, over a quarter of the entire series had mothers who may be said to have been old when the patients were born or who died prematurely.

It is interesting that the "shift to the right" of maternal age for psychotic patients is more pronounced than that reported for patients with achondroplasia by Bleyer [1] or for patients with congenital malformations by Murphy.[4] Moreover, the present series is larger than that of either of these writers, who nevertheless felt that their results, based on 303 and 607 cases respectively, were significant. By the same token, it is obvious that maternal age per se is unlikely to produce any specific effect on the offspring. Since it is represented in such diverse conditions as monstrosities, achondroplasia and psychoses, the ultimate cause of all these disorders must be sought elsewhere. In psychoses, as in the other conditions cited, advanced maternal age can be at most a predisposing or related factor.

With respect to the statistical treatment of results in this and in other studies cited, a word of caution is in order. There have been remarkable changes in the birth rates, as well as the death rates, during the past twenty years. In many cases, the total variation within a relatively short period has been more than 50 per cent.[17] For this reason, the conventional formulas for "reliability" are of doubtful value. Moreover, the composition of any community does not remain constant. Vital statistics are thus subject to change, as the populations which they represent are in a state of flux. For example, Pearl [18] and others have reported census figures showing that maternal ages were higher for foreign-born mothers than for mothers born in the United States. A statistical bulletin for the Metropolitan Life Insurance Company [19]

17. Mortality Improving More Rapidly Among Women, Statist. Bull. Metrop. Life Ins. Co. **21**:4-7, 1940.

18. Pearl, R.: Variation in Parity of Women Bearing Children in the U. S. Birth Registration Area in 1930, Human Biol. **9**:65-98, 1937.

19. Fertility of Foreign Born Women Thirty Per Cent Greater Than Native Born, Statist. Bull. Metrop. Life Ins. Co. **12**:6, 1931.

indicates that there have been marked fluctuations in the percentage of children born to older mothers during the past twenty years. During this interval the birth rate for native-born mothers over 40 years of age has been halved. For foreign born mothers, it has dropped to less than one third. It is hardly necessary to point out that a computation of probable errors for every group might be grossly misleading, unless the groups to be compared were born at substantially the same time as the original group, and, furthermore, unless the percentages of native-born and foreign-born mothers were similar. Instead of computing coefficients of reliability (which are, strictly speaking, valid only in terms of the population studied), I am, therefore, contrasting the percentage of mothers over 40 for my series of mental hospital patients with the percentage of older mothers for several other groups. This comparison is given in table 5.

TABLE 5.—*Percentages of Births at Maternal Age of over 40 in Present Series and in Series of Normal Persons Reported by Other Investigators*

Investigator	Cases	Place	Per Cent of Total Births in Which Mother Was 40 or Over
Anderson *	2,373	Cincinnati	1.8 (single births; live born)
Marston [5]	2,000	.....	2.1
Murphy [4]	1,584	Philadelphia	2.0 (normal children)
Guttmacher [3]	9,589	Baltimore	2.4 (all births)
Census figures		United States	3.88
Present study	1,000	psychotic patients	9.4

* Anderson, N. A.; Brown, E. W., and Lyons, R. A.: Causes of Prematurity, Am. J. Dis. Child. **61**: 72-87 (Jan.) 1941.

It will be noted that the percentage of mothers who were over 40 at the time they gave birth to a living child varies considerably among the normal groups, for reasons previously stated, but that it is much higher for the psychotic patients than for any of the normal groups reported. Of course, any statistical study cannot be accepted as final until it has withstood the test of independent confirmation. However, the evidence which is available indicates an excessive number of older mothers for mental hospital patients.

The second finding, namely, that many patients had experienced the death of their mothers during childhood, has been noted previously.[20] This finding has received some degree of confirmation in a paper by Rosenzweig and Bray.[21] Although these authors emphasize paternal mortality and are primarily concerned with schizophrenia, they present data which indicate that 7.2 per cent of their entire group of psychotic patients experienced the death of their mothers before they were 19, as compared with 2.5 per cent of a control group of normal persons. Both these figures seem low and might be increased if data had been available for all their subjects. Again, one sees the rather wide variation in percentages noted by different authors, which further emphasizes the need for caution in evaluating statistical findings.

The relation between psychosis and maternal mortality, as previously noted, might be interpreted in several ways: 1. Death of the mother might result in eventual psychosis in the offspring as a consequence of emotional trauma. 2. Death of the mother might result in a deterioration of the physical and emotional environment of the children. 3. An explanation might be invoked on a freudian basis in terms of disrupted family constellations and emotional tensions. 4. The relation might be incidental to some more immediate factor, such as the age of the mother (or even the age of the father). 5. Death of the mother might be evidence of deficient biologic stamina. This defect, if inherited by the children, might have as one manifestation the development of a psychosis.

The last possibility is consistent with the position taken by a number of investigators. Simms has written concerning a function which he designated as Q. This, Simms [22] asserted to be a measure of senile debility, both physical and mental, which also predisposes to a high death rate. He stated that superficial characteristics, such as condition of the hair and skin, are unsatisfactory criteria of senility. Indexes of unemployment and mortality rates he considered far more significant, according to mathematical equations which he worked out. Without passing on the validity of the equations which he proposed, it seems possible that mothers who died while in their twenties or thirties might be, *pari passu*, lacking in robustness or ruggedness, as in many cases they succumb to illnesses which are not fatal to a majority of women. In this connection, it is worth noting that the highest relative death rates for mothers of 1,000 mental hospital patients were among the younger mothers. Certainly, two phenomena noted for

20. Barry, H., Jr.: Study of Bereavement: An Approach to Problems in Mental Disease, Am. J. Orthopsychiat. **9**:355-359, 1939.

21. Rosenzweig, S., and Bray, D.: Sibling Deaths in Anamneses of Schizophrenic Patients, Arch. Neurol. & Psychiat. **49**:71-92 (Jan.) 1943.

22. Simms, H. S.: Physiological Alterations as the Cause of Senile Debility and Senile Mortality, Science **91**:7-9, 1940.

this group of psychotic patients—(1) a high rate of maternal bereavement, and (2) a disproportionate number of older mothers—might both be evidence of some biologic deficiency. However, any defect of these older mothers appears to have involved, primarily, their capacity to produce normal offspring, since their longevity compares favorably with normal persons or with younger mothers of psychotic patients.

A somewhat similar formulation which could account for both increased maternal age and increased mortality in mothers of psychotic patients has been discussed by Myerson [23] under the name "blastophoria." This makes use of a concept advocated by Adami [24] to the effect that germ plasm may be injured by environmental factors. Such injury has been demonstrated experimentally in animals by Stockard [25] and others. These investigators have shown that various forms of injury to the germinal epithelium may be antecedent to the appearance of defective offspring. It is, of course, possible that the degeneracy noted might be due to interference with normal embryonic development as a result of regressive changes either in the uterus or in the maternal blood stream, following debility or disease of the maternal organism.

While the foregoing discussion might apply to any of the disorders related to increasing maternal age, some progress has been made in tracing more specific relations between maternal age and two of the conditions previously noted. First, and most striking, is the discovery of the pathogenesis of erythroblastosis fetalis.[26] Since sensitization of the mother to the Rh factor normally occurs during pregnancy, a woman who has had numerous pregnancies is more likely to be sensitized; such a woman is also likely to be older. In this instance, the association between maternal age and erythroblastosis is apparently indirect. Another condition in which the relation between maternal age and a disease of the offspring is being formulated in terms of more specific pathogenic factors is mongolism. Benda[27] has postulated "noxious agents within the maternal organism" as being responsible for mongolism. These factors are supposedly related to endocrine disturbance within the mother. While his theories do not have the same degree of experimental confirmation as those which explained erythroblastosis fetalis, this is a stimulating approach. If his theory is correct, mongolism, as well as erythroblastosis, can be said to result from biochemical changes in the maternal organism which develop or become accentuated with age.

A number of incidental findings of this study are beyond the scope of the present paper. There is some evidence that fathers of patients at Greystone Park may have an older age distribution than fathers of normal persons (United States Census figures). It is possible that debility might operate through the paternal, as well as the maternal, germ plasm. In view of the well known hazards of statistical argument, it is hoped that these, as well as the major, findings presented in this report may be considered as preliminary—pending adequate confirmation.

SUMMARY AND CONCLUSIONS

1. Of 1,000 patients at a state hospital, 94 (9.4 per cent) had mothers who were over 40 years of age at the time of the patient's birth.

2. In the same series of patients, 174 (17.4 per cent) had mothers who died before the patients were 20 years old.

3. Paradoxically, there was a high death rate among the younger mothers, with a relatively low mortality rate among the mothers over 40 years of age.

4. In a preliminary series of psychoneurotic patients, the percentage of older mothers (3.6) was within normal limits.

23. Myerson, A.: Inheritance of Mental Diseases, Baltimore, Williams & Wilkins Company, 1925, p. 286.

24. Adami, J. G.: Medical Contributions to Study of Evolution, New York, MacMillan and Company, 1918; cited by Myerson.[23]

25. Stockard, C. R.: Physical Basis of Personality, New York, W. W. Norton & Company, Inc., 1931.

26. Levine, P.; Burnham, L.; Katzin, E., and Vogel, P.: Role of Iso-Immunization in the Pathogenesis of Erythroblastosis Fetalis, Am. J. Obst. & Gynec. **42**: 925-937, 1941.

27. Benda, C. E.: Endocrine Aspects of Mongolism, J. Clin. Endocrinol. **2**:737-748, 1942.

MÉNIÈRE'S SYNDROME

COMPARISON OF RESULTS OF MEDICAL AND SURGICAL TREATMENT

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The variety of treatments advocated for Ménière's disease is sufficient proof that the mechanism producing the attacks is not yet completely understood. Nevertheless, since good results are claimed for all methods, it has seemed that it would at least be interesting, and might be instructive, to compare the methods on the basis of published results.

MEDICAL TREATMENT

Table 1 shows the results claimed for various current medical treatments. All of these methods but one are predicated on clinical experiments made by their originators. Intravenous administration of histamine alone was a chance finding and is in that sense empiric. The usual criterion taken for success in treatment is relief of the attacks of vertigo. This varies rather widely in different series; but if the combined figures for relief and for marked improvement are taken, it is remarkable how closely the results coincide. In every series but one, more than 80 per cent of the patients were claimed to be greatly improved, the exception being the series of Walsh and Adson,[1] in which improvement was claimed to have been obtained in only 62 per cent with use of an accepted method not originated by the authors.

How can this rather unexpected finding be explained? The cynic may say that it is due to the predilection of a parent for his offspring—though, even so, it still seems strange that all the spectacles should be so uniformly tinted. The skeptic may suggest that the figures indicate not so much relief of vertigo as the natural tendency of the disease to remission, which notoriously makes computation of results difficult; but such prolonged remission or relief, though it may, and does, happen in individual instances, does not occur in 80 per cent of untreated patients. No doubt there is some error in all these figures due to this natural tendency of the disease to remission, but it may be called a constant variable. It could not well account for the great similarity in

TABLE 1.—*Results of Various Medical Treatments for Ménière's Syndrome*

Author; Treatment	Period of Observation	Number of Cases	Relief of Vertigo	Improvement of Vertigo	Improvement of Deafness	Improvement of Tinnitus
Mygind and Dederding,[5] 1934 (salt-free diet and dehydration)	Up to 3 yr.	157	43%	52% (95%)	17.4%	Not stated
Furstenberg,[6] 1934 (sodium-free diet plus ammonium chloride)	3 mo. to 7 yr.	35	57%	26% (83%)	9%	51%
Walsh and Adson,[1] 1940 (low salt diet plus ammonium chloride or potassium nitrate)	Up to 4 yr.	152	34%	28% (62%)	28%	"Essentially the same as deafness"
Talbott and Brown,[7] 1940 (high potassium diet)	1 mo. to 16 mo.	27	0%	96% "No acute attacks" (96%)	Not stated	"Some"
Lillie, Horton and Thornell,[11] 1944 (histamine intravenously)	1 mo. to 2 yr.	25	60% "While at clinic"	24% (84%)	48%	56%
Atkinson,[9] 1944 (nicotinic acid)	6 mo. to 3 yr.	110	38%	46% (84%)	23%	52%
Atkinson (unpublished) (histamine desensitization)	4 yr.	21	76%	14% (90%)	24%	38%

This paper was read at a joint meeting of the New York Academy of Medicine, Section of Neurology and Psychiatry, and the New York Neurological Society, March 13, 1945.

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1. Walsh, M. N., and Adson, A. W.: Ménière's Syndrome: Medical vs. Surgical Treatment, J. A. M. A. **114**:130 (Jan. 13) 1940.

the figures. There would seem to be two possible explanations. Either there is an unknown factor in the disease which has been overlooked by all the various investigators, or the pathologic process which produces the attack is such as could be influenced by each of these different measures, in its own particular way.

I do not want to speculate on a possible unknown factor, if there is one. Speculation plays too great a part in attempts to explain Ménière's syndrome as it is. The other possibility, that there is a common basic fault which is influenced by each of the current methods of treatment, seems a more plausible explanation. This basic fault could be an alteration in capillary permeability, which in cases of Ménière's syndrome involves particularly the capillaries of the stria vascularis in the labyrinth. This explanation has been advanced before by Brunner [2] and Portmann [3] and has in recent years received support from the histologic changes in a number of cases in which dilatation of the endolymphatic spaces has been shown (see Altmann and Fowler [4] for a complete review).

An increase in capillary permeability can be produced in one of two ways, either by anoxia from a diminished blood supply, which impairs the function of the capillary wall, or by sensitization to some foreign protein or chemical, as occurs classically in allergy, with the same result. In either case, seepage of serum takes place into the tissues, in the labyrinth into the endolymphphatic spaces. If this theory is accepted, the various treatments advocated and the consistency of the results make sense. One method of treatment restricts fluid intake (Mygind and Dederding [5]), and thus there will be less fluid to seep through the damaged capillary walls; another produces dehydration by administration of large doses of ammonium chloride (Furstenberg [6]) with the same result; another seeks to alter the electrolyte balance (Talbott and Brown [7]); others combat anoxia by producing vasodilatation (histamine,[8] nicotinic acid [9]) and so improve the function of the capillary wall; another produces desensitization in appropriate cases (histamine desensitization [10]) and seeks in this way to prevent and overcome the damage to the capillaries. This explanation is offered in no dogmatic spirit. It does, however, fit the known facts.

As to the merits of the various methods, I naturally favor my own. I find that I obtain results with them which I cannot obtain with the methods of others. This is probably in part because I have had more experience with them than with the others; in part also, no doubt, because I pursue them with more enthusiasm, but mainly, I am sure, because I attempt, however inadequately as yet, to group patients according to the cause of the syndrome and to treat them accordingly. One does well to remember that Ménière's syndrome *is* a syndrome and that its characteristic manifestations can be produced by several initiating factors. I find that the disease in patients who have been unsuccessfully treated with other methods can often be controlled when they are correctly grouped—but then, obviously, I see only my colleagues' failures, and not their successes, as they no doubt see mine. For instance, Dr. Madeleine Brown wrote me recently that she "continues to get good results in treatment of the acute form with potassium chloride." Yet I have several patients, some from Boston and environs, who have been treated with potassium chloride adequately and persistently with no, or only initial, success. I personally have tried conscientiously in the past all the methods enumerated in table 1, admittedly in small groups of patients only. I cannot approach the success which their authors claim for them. Indeed, only on rare occasions have I had any success at all. But I know that others say the same about my methods; so perhaps I have not been conscientious enough or persistent enough. Or perhaps each method has virtue in particular cases, and we physicians have not learnt enough to select cases correctly. But whatever may be the ex-

2. Brunner, H.: Die Pathologie und Therapie der vasomotorischen Erkrankungen des Innenohres, Wien. klin. Wchnschr. **38**:1235 (Nov. 12) 1925.

3. Portmann, G.: Vasomotor Affections of the Internal Ear, Ann. Otol., Rhin. & Laryng. **38**:69 (March) 1929.

4. Altmann, F., and Fowler, E. P., Jr.: Histological Findings in Ménière's Symptom Complex, Ann. Otol., Rhin. & Laryng. **52**:52 (March) 1943.

5. Mygind, S. H., and Dederding, D.: Diagnosis and Treatment of Ménière's Disease, Ann. Otol., Rhin. & Laryng. **47**:768 (Sept.) 1938.

6. Furstenberg, A. C.; Lashmet, F. H., and Lathrop, F.: Ménière's Symptom Complex: Medical Treatment, Ann. Otol., Rhin. & Laryng. **43**:1035 (Dec.) 1934.

7. Talbott, J. H., and Brown, M. R.: Ménière's Syndrome: Acid-Base Constituents of the Blood; Treatment with Potassium Chloride, J. A. M. A. **114**:125 (Jan. 13) 1940.

8. Shelden, C. H., and Horton, B. T.: Treatment of Ménière's Disease with Histamine Administered Intravenously, Proc. Staff Meet., Mayo Clin. **15**:17 (Jan. 10) 1940.

9. Atkinson, M.: Ménière's Syndrome: Results of Treatment with Nicotinic Acid in the Vasoconstrictor Group, Arch. Otolaryng. **40**:101 (Aug.) 1944.

10. Atkinson, M.: Histamine in the Treatment of Ménière's Syndrome: An Appraisal, J. A. M. A. **119**:4 (May 2) 1942.

planation, what is evident is that it is seldom that the vertigo cannot be controlled with medical measures of one sort or another.

Control of deafness and tinnitus is a different story. Tinnitus can be notably improved in some 50 per cent of all cases, and in a few it can be entirely relieved. Hearing, however, can be improved only in some 20 per cent of cases, and then not usually markedly, though in a small series Lillie and his collaborators,[11] using intravenous injections of histamine, obtained improvement in 48 per cent of cases. Usually the most that can be done is to hold the line and prevent a further loss. Damage done to hearing seldom can be undone.

great magnitude, for which good results are claimed by those that use it.[12] Portmann himself has never published any figures, as far as I can find out, but Waltner's [12b] are from his clinic. The concept is logical, but the operation has never "caught on."

Removal of foci of infection [13] is predicated on the theory that attacks of the Ménière syndrome are due to "toxic neuritis" of the eighth cranial nerve. The "focus" is usually to be found in some easily accessible organ, like the tonsil, the nasal sinuses or the teeth, and less often in an organ more difficult of attainment, like the gallbladder or the appendix. If one were to judge solely from the published figures, one would have to agree

TABLE 2.—*Results of Various Surgical Treatments for Ménière's Syndrome*

	Period of Observation	Number of Cases	Relief of Vertigo	Improvement of Vertigo	Improvement of Deafness	Improvement of Tinnitus
Operations on Eighth Nerve						
Coleman and Lyerly,[15] 1933	Not stated	10	100%	....	0%	100%
				100%		
Crowe,[14] 1938	Average 2.2 yr.	72	100%	....	19.5%	Not stated
				100%		
Walsh and Adson,[1] 1940	Not stated	20	65%	30%	Not stated	Not stated
				95%		
Operations on Labyrinth						
Mollison,[16] 1939	Not stated	50	74%	16%	Not stated	Not stated
				90%		
Cawthorne and Hallpike,[17] 1943	Up to 2 yr.	50	....	92%	22%	44%
				92%		
Day [19] 1944	1-3 yr.	8	75%	....	12.5%	75%
				75%		
Portmann Operation on Saccus Endolymphaticus						
Woodman,[12a] 1939	Not stated	11	73%	9%	5.5%	3%
				82%		
Waltner,[12b] 1940	Not stated	11	72%	9%	45%	18%
				81%		
Removal of Foci of Infection						
Wright,[13] 1940	More than 6 mo.	84	83%	5%	70%	50%
				88%		

SURGICAL TREATMENT

The various operations practiced fall essentially into two groups. One, the less common, consists of procedures predicated, like medical treatment, on a theory of causation; the other, and the more common, consists of operations of destruction on some part of the vestibular tract (table 2).

1. To take the less common group first, the Portmann operation seeks to overcome the increased production of endolymph by draining the labyrinth through the saccus endolymphaticus in the posterior fossa. It is an operation of no

that without a doubt this procedure is the answer to the problem both of causation and of treatment. Unfortunately, Wright stands a lone figure. His findings are against the weight of the evidence. Other workers in the field find no such prevalence of local infections (Crowe [14]).

11. Lillie, H. I.; Horton, B. F., and Thornell, W. C.: Ménière's Symptom Complex: Observations on Hearing of Patients Treated with Histamine, Ann. Otol., Rhin. & Laryng. **53**:717 (Dec.) 1944.

12. (*a*) Woodman, E. M.: The Position of the Portmann Operation in Relation to Labyrinthine Vertigo, Proc. Roy. Soc. Med. **32**:1642 (Oct.) 1939. (*b*) Waltner, J.: Le blocage du sac endolymphatique et l'opération de Portmann, Rev. de laryng. **61**:1 (Jan.) 1940.

13. Wright, A. J.: Further Clinical Observations on the Nature and Treatment of Ménière's Disease, Proc. Roy. Soc. Med. **33**:459 (June) 1940.

14. Crowe, S. J.: Ménière's Disease: A Study Based on Examinations Made Before and After an Intracranial Division of the Vestibular Nerve, Medicine **17**: 1 (Feb.) 1938.

They do not obtain the results from removal of tonsils, teeth and so forth that Wright has claimed. I myself, as a matter of routine, always look for a focus of infection. I scarcely ever find one. Nor have I ever found that removal of such a focus relieved the patient of his attacks, at least more than temporarily, in the way that tonsillectomy "cures" rheumatoid arthritis for a month or so; and I see many patients that have had this or that done to them before they reach me. If I have expatiated rather lengthily on this matter, it is because I believe that we physicians should set our faces against these nibbling operations, which in the general experience profit the patient not at all.

2. To turn now to the operations which are more commonly practiced, the operations of destruction, a different principle is encountered. Whereas medical treatment and the former group of operations attempt to overcome the assumed cause, these operations are concerned solely with preventing the effect. By dividing the conducting pathway, the vestibular nerve, or destroying the end organ in the labyrinth, they seek to prevent the stimulus from becoming effective. They do nothing to affect the stimulus itself. One may liken the state of affairs to an unwanted telephone conversation. These operations cut the wire or destroy the instrument so that the voice does not come through; they do not get rid of the speaker.

What, then, may be expected of surgical intervention? As far as section of the eighth nerve is concerned, the operation should theoretically be 100 per cent successful as regards relief of vertigo. So in practice it seems to be (Crowe,[14] Coleman and Lyerly[15] and Ray,[16] unreported series of 40 cases), provided—and the proviso is important—the diagnosis is correct and the operation complete.

If the diagnosis is incorrect, and if operation is performed in cases of paroxysmal vertigo not the result of labyrinthine disturbance, there will be distressing failures. I have in my records cases in which nerve section has been performed for paroxysmal vertigo which did not fulfil the criteria demanded for a diagnosis of Ménière's syndrome, and in which the condition was made not better but worse. Some of these cases come from a series in which 100 per cent success in surgical relief of vertigo was claimed. If the operation is incomplete failure again will occur, for which reason some surgeons (Ray) are tending to return to the older operation of total section of the nerve, holding it preferable to partial section, even though absolute deafness in the ear operated on is the price that must be paid. As to the other symptoms, hearing is seldom affected by section except for the worse, but tinnitus, strangely, is occasionally diminished, and even in rare instances relieved entirely, by section of the eighth nerve, either partial or complete.

Operations on the labyrinth differ somewhat in their results, depending on the particular procedure employed. The technics used are essentially of two kinds, one conservative and the other destructive. The first consists merely in opening the labyrinth, usually through the external semicircular canal (Cawthorne and Hallpike[17]); the second, in addition, employs injections of alcohol (Mollison[18]) or uses a coagulating current to destroy the whole, or a selected part, of the end organ (Day[19]). In general, relief of vertigo is less certain with this type of operation than with section of the eighth nerve; improvement in tinnitus and hearing, more usual with the conservative type. It is possible that, as more experience is gained with this type of operation and with the technical difficulties involved, it may come to supplant section as the the operation of choice. It is the more logical procedure.

But no matter what type of operation is to be performed, it is the general opinion of neurosurgeons, as well as otologists, that surgical intervention is to be regarded as the final resource. Not until medical treatment has been tried and failed should surgical therapy be advocated, except in special circumstances in which time is of primary importance and the diagnosis is without a doubt. Surgical measures can never offer as good results as can medical treatment at its best, which can on occasion procure a return to normal[9]; the results of surgical treatment are, however, more consistent and more rapid with regard to relief of vertigo.

CONCLUSION

The present position may be summarized as follows: Medical treatment can relieve or con-

15. Coleman, C. C., and Lyerly, J. G.: Ménière's Disease: Diagnosis and Treatment, Arch. Neurol. & Psychiat. **29**:522 (March) 1933.

16. Ray, B. S.: Unpublished results.

17. Cawthorne, T. E., and Hallpike, C. S.: Some Recent Work on the Investigation and Treatment of "Ménière's" Disease, Proc. Roy. Soc. Med. (Sect. Otol.) **36**:21 (Aug.) 1943.

18. Mollison, W. M.: Surgical Treatment of Vertigo by Opening the External Semicircular Canal and Injecting Alcohol, Acta oto-laryng. **27**:222, 1939.

19. Day, K. M.: Surgery of the Labyrinth for Ménière's Disease, Tr. Am. Acad. Ophth. (1943) **48**: 221 (March-April) 1944.

trol attacks of vertigo in some 80 per cent of cases; it can offer relief from or substantial improvement in tinnitus, a symptom which is often as distressing as vertigo, in some 50 per cent of cases; it can improve hearing to some extent in approximately 20 per cent of cases. Surgical treatment is to be regarded as a last resource when medical treatment has failed, but in selected cases it can be relied on to abolish vertigo; more should not be expected of it. It should always be remembered that operation is not entirely devoid of risk and that its results are irretrievable. Ménière's syndrome of itself is a benign condition, however distressing. It was not until the surgeons entered the arena that postmortem material became available for histologic study.

127 East Seventieth Street.

ELECTROENCEPHALOGRAPHIC LOCALIZATION AND DIFFERENTIATION OF LESIONS OF FRONTAL LOBES

PATHOLOGIC CONFIRMATION

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In dealing with intracranial lesions involving only the frontal lobes of the brain, the physician often is confronted with a paucity of neurologic evidence on which to base his judgment. Electroencephalography recently has been introduced as a procedure which, because of its applicability, appears to provide a partial solution of this problem. Although the electroencephalogram is utilized in the localization of lesions situated in various parts of the brain, this study is limited to those of the frontal lobes.

The question has arisen whether there are any characteristics in the abnormal electric activity of the cerebral cortex that would correlate with the underlying pathologic processes. A partial answer to this question is presented in this paper.

Since a detailed discussion of the literature is not included, the excellent reviews of Jasper,[1] Walter[2] and Gibbs and Gibbs[3] may be consulted. Walter[4] was the first to describe the accurate localization of cerebral tumors by means of the electroencephalogram as recorded from the surface of the scalp. He found slow random waves that were confined to the area of the head representing the site of the underlying tumor and called them delta waves. This term has been used to designate waves ranging from 1 to 7 cycles per second.[5]

TECHNIC

Electroencephalographic tracings were made with a four channel Grass balanced amplifier and an ink-writer that records on a paper tape moving at the rate of 30 mm. per second. The electrodes, 5 mm. in diameter, are stamped out of lead solder and are attached to the input terminals of the amplifiers by means of fine copper wires. These electrodes are filled with saline jelly and are fastened to the cleansed scalp of the patient with collodion. They are placed 5 cm. from the midsagittal line over the prefrontal, motor, anterior parietal, posterior parietal and occipital areas. The occipital electrodes rest 1.5 cm. in front of the inion. Electrodes are placed in the same manner over the temporal regions about 7 cm. directly above each external auditory meatus. In order to do both monopolar and bipolar recording, an electrode is attached to the lobe of each ear, and these two electrodes are connected to serve as a single reference lead. The electrodes on the head then become the specific leads. Suboccipital leads are utilized to help in distinguishing lesions of the cerebellum from those of the frontal lobes.

The conditions of recording are standardized as nearly as possible. The patients are placed on a bed in a semidarkened and electrically shielded room. They are instructed to lie as quietly as possible, with the eyes closed, but to remain in a waking state. Any sudden change in appearance of the electric waves prompts the technician to speak to the patient in order to prevent his falling asleep or drifting into a semidream state—two important factors which can produce certain interfering abnormalities in the wave pattern.

MATERIAL

This study is based on data concerning 100 consecutive patients, 67 men and 33 women, who had lesions of the frontal lobes of the brain. Each patient had a complete neurologic examination, including electroencephalographic recordings.[6] This series was selective

* At the time this study was made, Dr. Yeager was First Assistant in Neurology, at the Mayo Foundation.

This paper is an abridgment of a thesis submitted by Dr. Yeager to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Neurology and Psychiatry.

1. Jasper, H. H.: Electrical Signs of Cortical Activity, Psychol. Bull. **34**:411-481 (July) 1937.

2. Walter, W. G.: The Technique and Application of Electro-Encephalography, J. Neurol. & Psychiat. **1**: 359-385 (Oct.) 1938.

3. Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, Cambridge, Mass., Lew A. Cummings Co., 1941.

4. Walter, W. G.: The Location of Cerebral Tumours by Electro-Encephalography, Lancet **2**:305-308 (Aug. 8) 1936; The Electro-Encephalogram in Cases of Cerebral Tumour, Proc. Roy. Soc. Med. **30**:579-598 (March) 1937.

5. It is also proper to use the terminology of frequencies and potentials in referring to the various waves, although in this paper the original nomenclature has been retained to simplify description.

6. All electroencephalograms were read in the absence of any knowledge of the medical history or results of the neurologic examination of the patient. Usually the patient was not seen by the person who interpreted the record.

in that each lesion was confined to the frontal lobes, so far as it was possible to determine. Confirmation of all lesions was achieved either by surgical pathologic methods or by necropsy. Except for the aneurysms, all lesions in this series were verified microscopically.

In table 1 are indicated the types of lesions and the number of each type encountered.

TABLE 1.—*Types and Number of Lesions Encountered in 100 Cases of Lesions of the Frontal Lobe*

Type of Lesion	Cases
Spongioblastoma multiforme	31
Meningioma	26
Unclassified glioma	7
Neoplastic metastasis	7
Hemorrhage and infarct	6
Astrocytoma	6
Aneurysm	3
Oligodendroblastoma	3
Abscess	3
Astroblastoma	2
Oligodendroglioma	2
Ependymoblastoma	2
Ependymoma	1
Osteoma	1
Total cases	100

RESULTS

Forty-two of the 100 persons studied were shown by surgical intervention to have lesions involving the left frontal lobe. Forty-seven had lesions involving the right frontal lobe. Eleven had lesions involving both frontal lobes.

Table 2 shows the site of the delta localization in each case in which a focus was present. In 2 cases the results of the electroencephalographic examinations were normal in the presence of tumors.

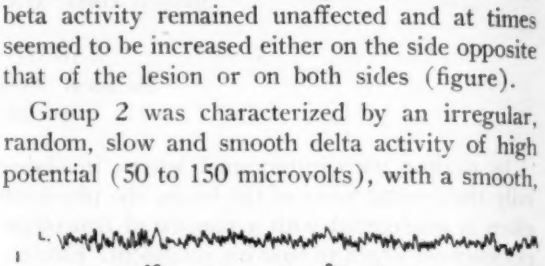
TABLE 2.—*Localization of Lesions as Indicated by Electroencephalograms*

Interpretation of Electroencephalographic Recordings	Total No.	Correct Area	Wrong Side	Electroencephalogram Misleading	Unlocalized Activity
Bilateral frontal delta localization	14	8*	..	..	..
Unilateral delta localization					
Frontal	35	24	1	..	..
Frontotemporal	31	30	1	..	..
Frontotemporoparietal	3	3	..	..	..
Frontoparietal	1	1	..	..	..
Temporal	3	..	..	3	..
Temperoparietal	1	..	..	1	..
Parietal	2	..	..	2	..
Temporo-occipital	2	..	..	2	..
Occipital	1	..	..	1	..
Generalized delta activity	4	..	..	..	4
Normal electroencephalogram	2	..	..	..	2
Indeterminate	1	..	..	..	1
Total	100	76	2	9	7

* In the remaining 6 cases the lesions were found at operation or necropsy to be unilateral, whereas our interpretation of the electroencephalogram had designated them as bilateral. Thus, these 6 cases do not represent either complete errors or complete successes and do not appear in either the "correct" or the "wrong" column.

The 100 electroencephalographic records were divided into three main groups. The first group was characterized by a relatively constant delta activity of from 3 to 6 cycles per second and of moderate potential (40 to 80 microvolts). The contour of the waves throughout the record presented considerable irregularity and sharpness. This delta activity was commonly confined to a single area as a rather circumscribed focus. When generalized delta activity was present, it was usually minimal and frequently was limited to one hemisphere. The occipital alpha rhythm was absent or reduced in amplitude. The frontal beta activity remained unaffected and at times seemed to be increased either on the side opposite that of the lesion or on both sides (figure).

Group 2 was characterized by an irregular, random, slow and smooth delta activity of high potential (50 to 150 microvolts), with a smooth, rounded, partially sinusoidal contour. Generalized delta activity was prevalent, and the beta rhythm of the frontomotor regions usually was abolished. There was a pronounced diminution or absence of the occipital alpha rhythm



Electroencephalographic tracings taken from the frontal regions (*L*, left; *R*, right) in cases of the following lesions of the brains: (*1*) Meningioma of the right frontal lobe. The delta activity is moderately slow and well circumscribed, with fast beta activity superimposed on it. The beta activity is predominant on the opposite side (a common finding). (*2*) Spongioblastoma multiforme of the right frontal lobe. The frequency is slow and the amplitude high. Normal frequencies are absent on the side of the lesion. There is considerable delta activity on the side opposite the lesion. The general picture is that of a slow, smooth type of wave. This suggests severe damage. (*3*) Astrocytoma of the left frontal region, with a cyst filled with fluid. Note the rhythmic, high amplitude, sinusoidal chain of waves. They were frequently found with cystic lesions and with abscesses. (*4*) Old hemorrhage of the left frontal lobe. Note the low amplitude waves with considerable variation of frequency. In this case there are some spontaneous waves—both alpha and beta.

on the side of the lesion. In most instances the electric activity of the opposite cerebral hemisphere was involved, with a partial decrease of the occipital alpha activity.

Group 3 included those records which are less easily described and classified. These records presented a more or less heterogeneous pattern, often described as ragged and choppy. The delta activity noted was of low potential and variable in frequency with superimposed alpha and beta activity. The spontaneous alpha and beta waves, whether superimposed or in areas free of delta activity, were sparse, of low potential and irregular in form.

In 19 (73 per cent) of the 26 cases of meningioma, the wave pattern was found to be in electroencephalographic group 1. In 6 cases (23 per cent), in all of which the tumor was shown microscopically to be of the malignant cellular type, the delta activity was in electroencephalographic group 2, and in 1 (4 per cent) it was in electroencephalographic group 3.

In the 1 case of osteoma of the frontal bone, pressing on the cerebral cortex, the delta activity had the characteristics of electroencephalographic group 1. This wave pattern resembled that seen with the meningiomas and may be explained by the similar cortical changes produced by meningiomas and osteomas.

In 43 (80 per cent) of the 54 cases of glioma the wave patterns were in electroencephalographic group 2; in 8 cases (15 per cent), in group 3, and 1 case (2 per cent), in group 1. Of the 2 remaining cases of glioma, a circumscribed epileptogenic focus of low potential in the motor area was present in 1, and asymmetry, with reduced alpha activity on the side of the lesion, in the other.

Of the 12 cases of non-neoplastic lesions of various types (hemorrhage, infarct, abscess and aneurysm), the wave patterns in 7 (58 per cent) were found to be in electroencephalographic group 3; in 2 cases (17 per cent), in group 1, and in 3 cases (25 per cent), in group 2.

In 5 (71 per cent) of the 7 instances of neoplastic metastasis the records were in electroencephalographic group 2, and in 2 (29 per cent), in group 3.

The pattern of the electroencephalograms in group 1 was found to be associated with meningiomas in the majority of cases, and the pattern in group 2 was identified with gliomas of all types (table 3). The intensity of the changes in the record depended in part on the nature and extent of the lesion. The changes were most pronounced in the presence of spongioblastoma multiforme. When the existing lesion contained cystic cavities, an additional wave pattern of high potential, sinusoidal waves of 2 to 3 cycles per second appearing in intermittent sequences was frequently found. The wave form characteristic of abscesses resembled closely the wave form characteristic of cystic lesions except for less obvious sinusoidal sequences. For the most part metastatic lesions produced electric patterns resembling those of gliomas. Vascular lesions presented a pattern similar to that seen in group 3.

In evaluating changes in the records according to these classifications, it should be emphasized that such groupings are arbitrary and may overlap, so that some of the characteristics of all the groups may be found in a single record.

The interpretation of each record depends on a number of variable factors. One should always consider the wide range of normal variations in the electroencephalogram. The electric potentials of young persons are higher than those of older persons; thus a lesion in a young person might produce a record having a fairly strong alpha rhythm and a high potential delta activity, whereas an equally damaging lesion in an older person might produce a less persistent alpha rhythm and a somewhat lower potential delta activity. The more rapidly growing tumors tend to produce higher potentials and slower frequencies than do the more slowly growing tumors. Thus, the malignant meningiomas produced a wave pattern similar to that of the gliomas. The final analysis is determined by an evaluation of the record as a whole. A comparison is made of the wave forms from all regions of the head.

This evidence indicates that by means of the electroencephalogram one can ascertain the kind of cerebral pathologic process to a limited degree.

TABLE 3.—*Lesions as Found at Operation or Necropsy Compared with Lesions as Suggested by Nature of Delta Waves Before Operation in 100 Cases of Lesions of the Frontal Lobes*

		Estimated Type of Delta Wave in Electroencephalogram					
		Group 1		Group 2		Group 3	
Lesion Found to Be	Total No.	No.	Per Cent	No.	Per Cent	No.	Per Cent
Meningioma	26	19	83	6	10	1	6
Glioma	54*	1	4	44†	76	8	44
Non-neoplastic	12	2	9	3	5	7	39
Neoplastic metastasis	7	..	..	5	9	2	11
Osteoma	1	1	4	..	..	..	..
Total number	100	23	100	58	100	18	100

* One glioma showing an epileptogenic focus did not fit into any of the groups.

† This group includes 43 records and 1 record which, because of the reduced alpha activity, is included here with group 2.

COMMENT

By coagulating the cortex of monkeys, Dusser de Barenne and McCulloch[7] proved that the electric potentials arise from the neurons of the cerebral cortex. Schwartz and Kerr,[8] as well as Scarff and Rahm,[9] studied the electric potentials obtained from the exposed brain in the presence of tumors. These studies explain why the pathologic character of the lesion can be ascertained to a limited extent by the delta pattern. They showed that in all instances the tumor tissue was inactive and that the effect of the tumor on the surrounding cortical tissue was the basis of the production of potentials of high amplitude and slow frequency. Scarff and Rahm demonstrated that the damage to portions adjacent to benign and encapsulated tumors was small and that there was slight or no retardation of the spontaneous cortical waves. Conversely, malignant and invasive tumors, such as spongioblastomas, were shown to damage the surrounding brain tissue over a much wider region, destroying the normal, spontaneous electric activity. There was a tendency for normal potentials to reappear remote from the tumor mass.

In the cases of meningioma considered in this paper the delta focus was circumscribed and the beta activity, frequently characteristic of the frontal regions, was found to be altered only slightly, if at all. In contrast, in the cases of glioma there was a widespread, slow, high potential type of delta wave with pronounced destruction of the spontaneous electric activity.

The observations of Walter, Griffiths and Nevin[10] substantiated the impression that the generalized delta activity is a result of injury to subcortical centers by invasive tumors. Walter and his associates studied a case of hypothalamic tumor associated with a pathologic disturbance of sleep which produced diffuse, slow, random delta waves even though the cortex and the white matter were normal. This observation may account for the rather pronounced generalized delta activity associated with the spongioblastomas. This activity appears to be secondary to a remote influence occasioned by damage to the deeper centers. In contrast, the benign meningiomas give rise to a more moderate form of diffuse delta activity because of less damage to deep centers.

The work of Bucy and Case[11] tends to confirm the belief that disruption of the occipital alpha rhythm may be caused by interference with the conduction of impulses over the association fibers. Bucy and Case noted that unilateral loss of occipital alpha activity, when associated with homonymous hemianopsia, is the result of destruction of the optic radiations. Here the alpha rhythm is considered a cyclic electric phenomenon circulating in a chain of neurons, one link of which is the optic radiations. Although homonymous defects were not noted generally, other neuron systems in the transcerebral association mechanisms could well account for the disrupted alpha rhythm in the cases considered in this paper.

The aforementioned observations of Walter and his group[10] and those of Bucy and Case also might explain why in 6 of the cases of unilateral spongioblastoma multiforme bilateral frontal delta localizations with loss of spontaneous electric activity were observed. The invasion of the neoplasm damages the transcerebral fibers of the corpus callosum as well as the deeper brain centers. This damage interrupts the intracerebral electric circuits, so that abnormal waves appear in the opposite frontal cortex.

In many of the cases in which choked optic disks were noted, there was moderately high potential, sinusoidal electric activity of 5 to 6 cycles per second. This activity was usually intermittent and frequently was associated with the slower, less regular type of generalized delta activity. We were impressed with the idea that this wave pattern somehow was related to increased intracranial pressure, as manifested clinically by choking of the optic disks. Walter, in further discussing his case of hypothalamic tumor, distinguished the slow, high potential, irregular waves caused by this lesion from the somewhat faster and lower potential waves associated with edema of the brain. Williams[12] attributed the rhythmic, moderately slow electric activity, which was distributed uniformly over the cerebral cortex, to interference with conduction of the fiber tracts as a result of edema of the

7. Dusser de Barenne, J. G., and McCulloch, W. S.: Some Effects of Laminar Thermocoagulation upon the Local Action Potentials of the Cerebral Cortex of the Monkey, Am. J. Physiol. **114**:692-694 (Feb.) 1936.

8. Schwartz, H. G., and Kerr, A. S.: Electrical Activity of the Exposed Human Brain: Description of Technic and Report of Observations, Arch. Neurol. & Psychiat. **43**:547-558 (March) 1940.

9. Scarff, J. E., and Rahm, W. E., Jr.: The Human Electrocorticogram, Tr. Am. Neurol. A. **66**:20-25, 1940.

10. Walter, W. G.; Griffiths, G. M., and Nevin, S.: The Electro-Encephalogram in a Case of Pathological Sleep Due to Hypothalamic Tumour, Brit. M. J. **1**:107-109 (Jan. 21) 1939.

11. Bucy, P. C., and Case, T. J.: An Association Between Homonymous Hemianopsia and Unilateral Absence of the Alpha Waves, Tr. Am. Neurol. A. **66**: 17-20, 1940.

12. Williams, D.: The Abnormal Cortical Potentials Associated with High Intracranial Pressure, Brain **62**: 321-334 (Sept.) 1939.

white matter. This activity seems to be similar to that associated with edema of the brain, as described by Walter and others.[10] The edema depends on an alteration of water balance or ionic concentration in the tissue, that is, a disturbance of the osmotic pressure of the cellular tissue in the white matter of the hemispheres. The cortex is not involved.

Again, in the cases in which choking of the optic disks was present, there was demonstrated a rhythmic electric activity of 5 to 6 cycles per second, as well as slower, irregular, diffusely distributed delta waves. On this basis, the hypothesis might be established that two factors exert an influence on the combined electroencephalographic picture: first, edema of the white matter, producing the rhythmic wave form by partially interfering with the neuronal conduction, and, second, the conduction of impulses over fiber tracts from remote areas, producing slow, irregular, generalized delta activity.

SUMMARY

In a review of 100 consecutive cases of verified lesions of the frontal lobes of the brain in which electroencephalographic recordings were made, the procedure was found to be valuable in localization of the lesion because of its simplicity and ready applicability. By utilizing the information gained from the electroencephalogram, one may obtain a clue to the pathologic nature of the underlying lesion.

SCHIZOPHRENIC REACTION SYNDROME IN COURSE OF ACUTE DEMYELINATION OF CENTRAL NERVOUS SYSTEM

CLINICOPATHOLOGIC REPORT OF A CASE, WITH BRIEF REVIEW OF THE LITERATURE

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There is much controversy among various authors concerning the clinical diagnosis of certain schizophrenic syndromes which are associated at times with doubtful neurologic signs and with which definite organic changes in the brain appear. This difference of opinion arises from the fact that some authors explain the mental symptoms on the basis of psychogenic mechanisms while others believe that these symptoms may be the expression of organic changes.[1]

It seems to us that it is of interest and importance that both clinicians and neouropathologists take into consideration the fact that, besides psychogenic mechanisms, various somatogenic factors, acting independently or in combination, may precipitate a schizophrenic syndrome.[2]

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1. Alzheimer, A.: Beiträge zur pathologischen Anatomie der Dementia Praecox, Ztschr. f. d. ges. Neurol. u. Psychiat. **7**:621, 1913. Cotton, H. A.: Fatty Degeneration of the Cerebral Cortex in the Psychoses, with Special Reference to Dementia Praecox, J. Exper. Med. **22**:492, 1915. Josephy, H.: Beiträge zur Histopathologie der Dementia Praecox, Ztschr. f. d. ges. Neurol. u. Psychiat. **86**:391, 1923. Fünfgeld, E.: Ueber die pathologische Anatomie der Schizophrenie und ihre Bedeutung für die Abtrenung "atypischer periodisch verlaufender Psychosen," Monatschr. f. Psychiat. u. Neurol. **63**:1, 1927. Buscaino, V. M.: Ricerche istoneuropatologiche, encephalografiche e del liquor in dementi precoci (con un'appendice sulle "zolle di disintegrazione a grappolo"), Riv. di pat. nerv. **34**: 181, 1929. Hechst, B.: Zur Histopathologie der Schizophrenie, Ztschr. f. d. ges. Neurol. u. Psychiat. **134**:163, 1931. Freeman, W.: Lipoid Degeneration Products in the Thalamus and Globus Pallidus in Schizophrenia with a Note on Calcification, A. Research Nerv. & Ment. Dis., Proc. **5**:382, 1928; Deficiency of Catalytic Iron in the Brain in Schizophrenia, Arch. Neurol. & Psychiat. **24**:300 (Aug.) 1930. Ferraro, A.: Histopathological Findings in Two Cases Clinically Diagnosed Dementia Praecox, Am. J. Psychiat. **13**:883, 1934. Elvidge, A. R., and Reed, G. E.: Biopsy Studies of Cerebral Pathologic Changes in Schizophrenia and Manic-Depressive Psychoses, Arch. Neurol. & Psychiat. **40**:227 (Aug.) 1938. Bruetsch, W. L.: Chronic Rheumatic Brain Disease in Schizophrenia, Am. J. Psychiat. **97**:276, 1940; Late Cerebral Sequelae of Rheumatic Fever, in Annual Report of the Central State Hospital, Indianapolis, Ind., 1943. Kirschbaum, W. R., and Heilbrunn, G.: Biopsies of the Brain of Schizophrenic Patients and Experimental Animals, Arch. Neurol. & Psychiat. **51**:155 (Feb.) 1944.

2. (*a*) Bleuler, E.: La schizophrenie, Rev. neurol. **2**:474, 1926; (*b*) Textbook of Psychiatry, New York, The Macmillan Company, 1930. (*c*) Menninger, K. A.: The Schizophrenic Syndrome as a Product of Acute Infectious Disease, A. Research Nerv. & Ment. Dis., Proc. **5**:182, 1928. (*d*) Campbell, M. C.: On the Definition or Delimitation of Schizophrenic Type of Reaction, ibid. **5**:16, 1928. (*e*) Hutchings, R.; Cheney, C. I., and Wright, W. W.: Psychogenic Precipitating Causes of Schizophrenia, ibid. **5**:159, 1928. (*f*) Jelliffe, S. E.: The Schizophrenic Group, J. Nerv. & Ment. Dis. **74**:347 and 543, 1931. (*g*) May, G. V.: The Dementia Praecox–Schizophrenia Problem, Psychiatric Quart. **6**:40, 1932. (*h*) Courtois, A., and Borel, J.: Encéphalopathie de l'enfance, Syndrome de démence précoce, Rev. neurol. **1**:299, 1932. (*i*) Courtois, A.: Certains agents étiologiques des syndromes de démence précoce, Ann. méd.-psychol. (pt. 2) **93**:51, 1935. (*j*) Goldstein, K.: Zur pathologischen Anatomie der Dementia praecox im besonderen der plötzlichen Todesfalle bei derselben, Monatschr. f. Psychiat. u. Neurol. **25**:565, 1909. (*k*) Kronfeld, A. S.: Schizophrenia-like Psychosis in Patients with Organic Brain Disease, Sovet. psikhonevrol. **16**:92, 1940. (*l*) Shapiro, L. B.: Schizophrenic-like Psychosis Following Head Injuries, Elgin State Hosp. Papers **4**:153, 1941. (*m*) Kimball, I.: Schizophrenic and Organic Reaction Type of Psychoses, Kentucky M. J. **41**:346, 1943. (*n*) Polatin, P.; Eisenstein, V. W., and Barrera, S. E.: Organic Psychosis Simulating Dementia Praecox, Psychiatric Quart. **18**:391, 1944.

In support of this view, we shall limit ourselves to presenting and discussing one type of organic cerebral change which may precipitate clinical manifestations of the schizophrenic type.

REPORT OF CASE

B. G., a 34 year old married white woman, a factory worker, entered the New Hampshire State Hospital on Jan. 9, 1942, on a regular commitment. Three weeks previously the patient had begun to complain of "trouble with her throat." She spoke in a whisper and stated that she was unable to talk out loud. Examination by an otolaryngologist revealed nothing abnormal. Four days later the patient appeared unable to speak at all and could not, or would not, eat or swallow. When taken to a general hospital, she seemed to recognize people about her and wrote brief notes to communicate with them. However, she soon became restless, slept poorly and had to be fed with a tube. Examination by a neuropsychiatrist at this time revealed that she was "listless" and at times "exhibitionistic, uncovering and exposing herself." This specialist indicated, also, that the patient was "quite aware of her environment." Neurologic examination at that time was reported to reveal an essentially normal condition except for active tendon reflexes and absence of plantar, abdominal and corneal reflexes. No signs of bulbar paralysis were elicited; the condition of the spinal fluid was within normal limits. The patient was committed with a diagnosis of "major hysteria (?), catatonia."

Personal History.—Birth and early development were normal. The patient graduated from grammar school at the usual age. Shortly afterward she went to work in a shoe factory and continued at that occupation until her present illness. She was married at the age of 21 to her present husband. The only child of the union died at the age of 2 years, of pneumonia. The patient showed a normal amount of grief at her child's death. Aside from mild neurotic traits, she showed no psychopathologic manifestations until the onset of the present illness. The medical history was noncontributory except that during the past three years the patient had been bothered with occasionally "losing her voice." This disturbance would last only a day or so and would then disappear as rapidly as it had come.

Family History.—There was no family history of nervous or mental disorder except that an older brother had been hospitalized three years previously for a condition diagnosed as dementia paralytica. Despite malarial fever treatment, he died of this disorder two months after admission. Autopsy was not performed.

Physical Examination.—On admission the patient was asthenic, rather poorly nourished and somewhat dehydrated. The blood pressure was 120 systolic and 82 diastolic, the temperature 99.6 F., the pulse rate 104 and the respiration rate 22.

Neurologic Examination (in consultation).—The report follows: "The patient understood the meaning of questions and was able to answer simple questions by sign language. She was slightly resistive when asked to open her mouth or to smile. The disks were clearly outlined. The blood vessels were of normal caliber. The motor system was normal. Vibration sense was reduced on the left, but the results were hard to evaluate.

"Reflexes: The biceps and triceps reflexes were 1 to 2 plus; the knee jerk was 2 to 3 plus, and the ankle jerk, 1 plus; an ankle clonus was elicited on the left. Abdominal reflexes were not elicited. No abnormal reflexes were obtained.

"Impression: No evidence of local damage to patient's nervous system was found. The aphasia was not typical of organic disease of the brain and probably was on a schizoid or hysterical basis."

Laboratory Data.—The Hinton reaction of the blood was negative; the blood count was normal throughout. Urinalysis gave normal results except for a positive reaction for acetone. Examination of the spinal fluid had been previously reported as showing nothing abnormal.

Mental Status and Course in the Hospital.—The patient was cared for in the admission ward during her entire stay in the hospital. She remained in what appeared to be a catatonic stupor. Thus, most of the time she would lie in bed staring with a wooden expression at the ceiling and not responding to ordinary stimuli. Occasionally she showed impulsive behavior. Thus, she would throw off her bedclothes in an exhibitionistic way. A few times she tore off the clothing for no apparent reason and with no regard for who might observe her. For the most part it was difficult or impossible to obtain her attention or to make contact with her. However, once in a while, when her attention was obtained, she would gesture toward her throat and would stroke it with both hands, as though trying to indicate that the site of the trouble was there. During the first part of her stay in the hospital psychomotor activity was increased for short periods. During these episodes the patient moved restlessly about the ward, annoying the other patients, although she took little notice of them. Her facial expression was bewildered and perplexed. After a few days she refused to get out of bed and refused food. When an attempt was made to urge her to take nourishment, she became resistive. The most she would ever do was to swallow a few sips of milk. Thus it became necessary to feed her by tube daily.

At no time during her stay in the hospital did the patient speak audibly, but during the first week she would occasionally try to form words with her lips. Emotionally she appeared somewhat depressed; her manner was preoccupied and withdrawn. On one or two occasions she showed flashes of apprehension. These reactions were apparently motivated from within.

Because of her muteness, no idea of her mental content could be obtained. On the basis of observations, she seemed to be reacting to auditory hallucinations, in that she at times showed an attitude which might be described as listening. Although it was impossible to evaluate the state of her sensorium precisely, it appeared evident that she recognized persons about her, at least during the first week of her stay in the hospital, and that she appreciated the fact that she was in a hospital.

On the assumption that hysterical elements might be present, hypnotism was tried first in the treatment of her disorder, but she remained entirely resistant to this form of therapy. Likewise, her condition appeared quite unaffected when 15 grains (0.975 Gm.) of sodium amytal was given intravenously. After a week's study, the patient was given a course of three metrazol convulsion treatments. Despite this, her clinical condition remained basically unchanged, and the treatments accordingly were discontinued. Tube feedings had to be maintained. The patient tended to gag and cough rather excessively with each feeding. Two weeks after admission a moderate fever with a rectal temperature of 102.5 F. developed, and signs of patchy consolidations appeared in the lungs. She failed rapidly and died on January 24. The clinical

cause of death was given as bronchopneumonia due to aspiration, with inanition as a contributing cause.

Summary.—The patient was a 34 year old white woman with no past history of mental or nervous illness and an apparently negative family history in this respect. The illness in question was noteworthy for its extreme suddenness of onset, the lack of response to shock treatment and the rapidly fatal course.

In view of the increased psychomotor activity (in the beginning of the illness), followed by negativism, some stereotopy, resistiveness, mutism, refusal to eat and a rapid downhill trend, most staff members of the New Hampshire State Hospital felt that the clinical course in this case resembled schizophrenia of the catatonic type.

However, at the very onset of the clinical symptoms there was a question of major hysteria, as suggested by mutism, apparent inability and refusal to swallow and apparent aphonia. In favor of such an evaluation of the symptoms was the absence of any motor defects of the tongue, lips or larynx and absence of outbursts of laughing and crying, so often observed with the supranuclear type of palsy.

Even though left ankle clonus and somewhat increased patellar reflexes were present, in addition to the absence of corneal and abdominal reflexes, two neurologists who were called in consultation stated the belief that the clinical picture was not to be considered that of a neurologic disorder. On such grounds and because the mental symptoms dominated the clinical picture, the diagnosis of schizophrenic syndrome, catatonic type, was retained throughout the life of the patient.

Autopsy.[3]—The gross pathologic changes consisted of (1) multiple, small abscesses of both lungs; (2) several areas of a purulent inflammatory process over the pleura of the lower lobes of both lungs, and (3) apparently normal meninges and brain. However, in one section of the brain a number of small, bilateral, roughly symmetric areas, almost serpiginous in outline, were found in the subcortical regions of the frontal and parietal lobes (fig. 1). The consistency of such areas was peculiarly gelatinous. A few similar areas were noticed likewise in the medulla near the pons. Otherwise, the brain appeared grossly normal.

Microscopic examination confirmed the presence of small abscesses in the lungs and an acute inflammatory exudate over the pleura. Smears from the pulmonary abscesses showed various types of both rod and coccus forms of bacteria.

Microscopic Examination of Central Nervous System.—Blocks from the prefrontal, frontal, parietal and temporal cortex, the basal ganglia and the medulla were studied after fixation in alcohol and diluted solution of formaldehyde U. S. P.. The usual neuropathologic technics were employed, as well as some histochemical reactions for fatlike substances and myelin products of disintegration.

With stains for myelin sheaths, considerable demyelination involving in variable degree most parts of the white matter of the frontal and parietal lobes bilaterally and symmetrically was observed. Some of the demyelinated areas appeared sharply outlined, whereas others less well demarcated assumed the aspects of the "transitional type" of demyelination. Generally, these demyelinated areas were limited to the subcortical white matter, but occasionally the U fibers and the deep cortical layers were involved. In certain instances the irregular appearance and distribution of the demyelination reproduced roughly the aspect of Marburg's "geographic map-like" variety of demyelination.

The intensity of the demyelination was irregular (fig. 2 *A*). In some areas there were only rarefaction, swelling and slight degeneration of the myelin sheaths. In others the demyelination was almost complete, and only here and there remnants or debris of disintegrated myelin sheaths were noticeable. In others, finally, various stages of transitional alterations were encountered

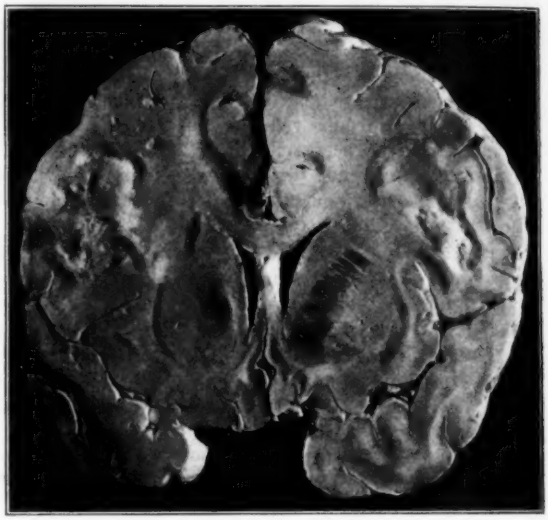

Fig. 1.—Coronal section of the fixed brain through the basal ganglia, revealing the presence of subcortical, bilateral and roughly symmetric areas of softening, of irregular outline; approximately one-half natural size.

(fig. 2 *B* and *C*). In a few areas bands of less intense damage to the myelin alternated with bands of almost complete destruction of myelin, recalling Baló's concentric type of demyelination. Such areas were more distinct when the lipid material was dissolved (fig. 2 *C*).

In the medulla oblongata two small areas of demyelination were present. They were not limited by any anatomic topography.

Some of the demyelinated areas were localized around or near blood vessels (veins or arteries), but in many instances, particularly in the regions of alternating demyelination, no relation to the vascular pattern could be found.

Combined methods for nerve fibers and myelin sheaths revealed that axis-cylinders appeared more resistant than the myelin sheaths. Where the myelinolysis was more severe, scarcely any nerve fibers were left, but only fragments and debris surrounded by large macrophages containing granular material formed by disintegration of myelin; where the demyelination was less intense, more

3. Autopsy was performed by the late Dr. David Dial, of the New Hampshire State Hospital.

axis-cylinders were present, and closer to the borders of the lesions an increasing number of nerve fibers were present and preserved.

Various histochemical methods revealed that the staining and histochemical properties of the fatlike substances and the products of myelin disintegration varied not only from one area to another but at times in the same area. In the areas in which a large amount of fat was present, the substance assumed the form of condensed material free in the tissue or accumulated in compound granular corpuscles (fig. 3 *A*). The perivascular spaces, as well as the adventitial sheaths of the blood vessels, were also laden with many scavenger cells filled with fat material.

However, the so-called argyrophil granules were seen mostly intracellularly in elements having the appearance of large, granulated macrophages (fig. 3 *B*). In the areas where the fatlike substance and products of myelin disintegration were present in less quantity, the material occurred more frequently intracellularly and surrounding the perivascular spaces of some blood vessels. In addition, in some of the involved areas, particularly in the medulla, metachromatically stained bodies were also observed.

We should like to mention only that this variety of histochemical reactions of the fatlike substances and products of degeneration is, in our opinion, related to difference in stage of myelin disintegration.

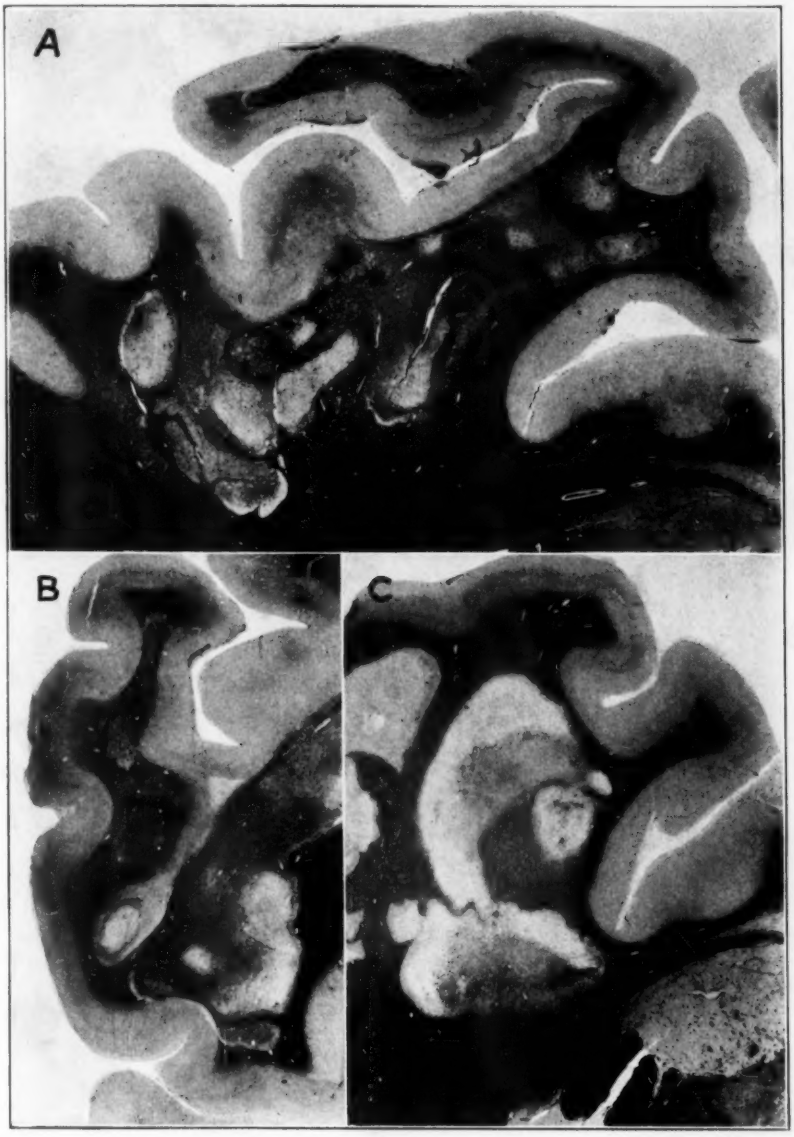

Fig. 2.—*A*, *B* and *C*, multiple, irregular and transitional type of demyelination, as described in the text; Roizin's combined method for myelin sheaths and lipid products of disintegration; low power magnification.

The distribution and intensity of the macroglial reaction were heteromorphic in character and almost inversely proportional to the process of demyelination. But this was not always the case, for it was also observed that in certain areas of severe destruction of myelin and in areas where the process appeared to be of more recent character the glial proliferation was lacking or was not proportionately so intense as would be expected.

Several cytologic methods revealed in the demyelinated areas various degrees of perivascular infiltration. The amount and the character of the cellular elements surrounding the blood vessels varied from area to area: At times the perivascular cuffings consisted of lymphocytes; at others, of gitter cells, and at still others, of a mixture of gitter cells, lymphocytes, large mononuclear cells and plasma cells (fig. 4 *A*). Occasionally, granulomatous formations, composed mostly of lymphocytes and large mononuclear cells, were also observed (fig. 4 *B*). In addition, mixed with the perivascular elements or free in the interstitial tissue, large globoid cells with three or four nuclei were seen scattered here and there (fig. 4 *C* and *D*).

At times small hemorrhages surrounding blood vessels were also encountered (fig. 5 *A*); at others red blood cells were mixed with the perivascular inflammatory elements (fig. 5 *B*). Although the inflammatory cuffings had generally a perivascular distribution, on several occasions the walls of the blood vessels were infiltrated.

In certain instances, the walls of the blood vessels disclosed fibrous thickening of the adventitia or media or hyaline degeneration. Many of the endothelial cells of the infiltrated vessels had swollen nuclei.

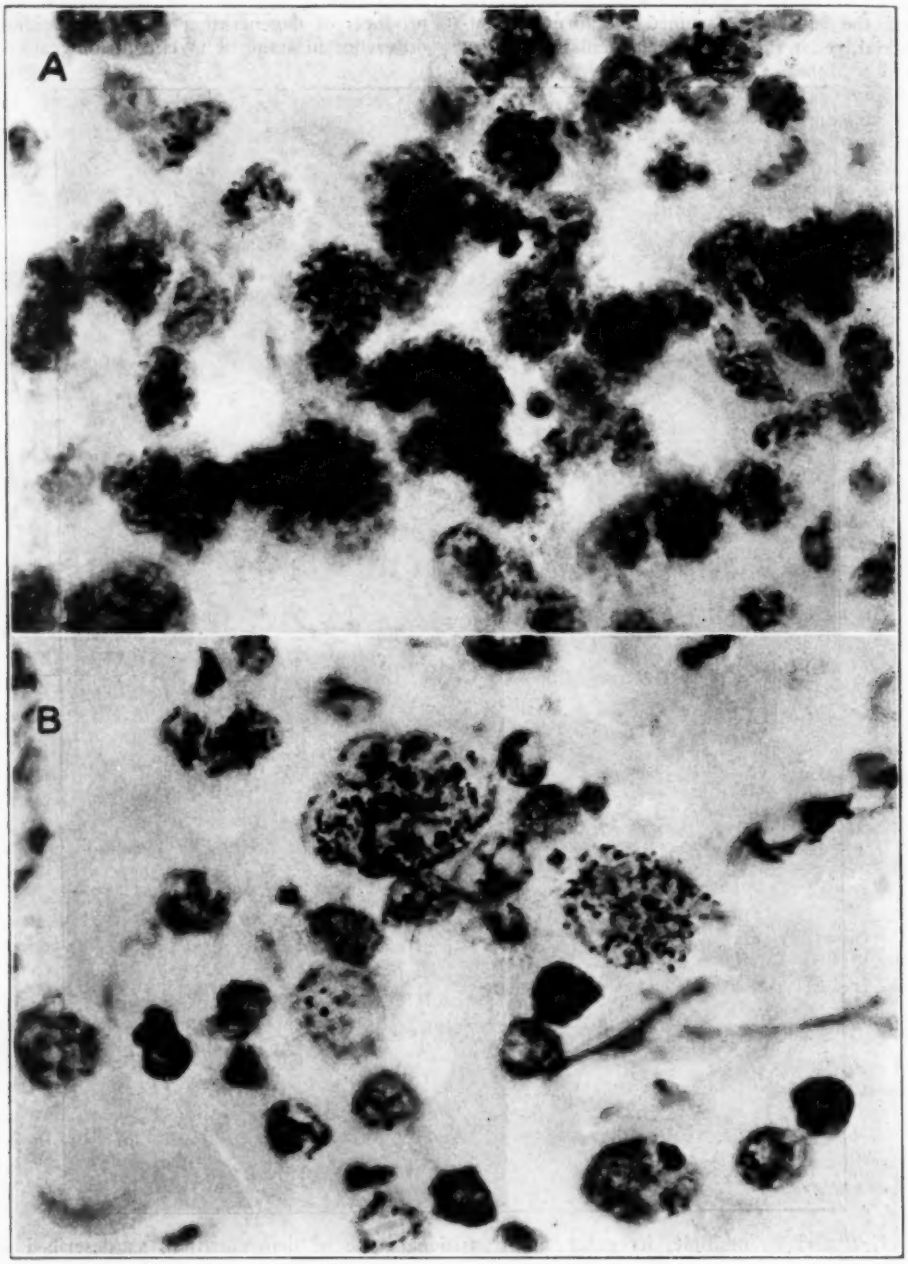

Fig. 3.—*A*, compound granular corpuscles, containing various types of lipid products of disintegration; Roizin's combined method for myelin sheaths and lipid products of disintegration. *B*, large phagocytic elements, containing argentophil granular material; ammoniacal silver method; high power magnification.

With the common methods no definite thrombosis was observed.

The cytologic methods did not reveal any appreciable cytoarchitectonic alteration of the cortex, although here and there the presence of individual cells or of groups of cells undergoing tigrolysis, chromatolysis and neuronophagia was noticed. These cellular changes were more frequently observed in the third and fifth layers of the prefrontal, frontal and temporal cortical regions. Occasionally, in the same regions, more severe neuronal changes, as well as small acellular areas, were found. In the middle and deeper cortical layers, as well as in the subcortical zone, numerous oligodendrocytes in the stage of acute swelling were also detected.

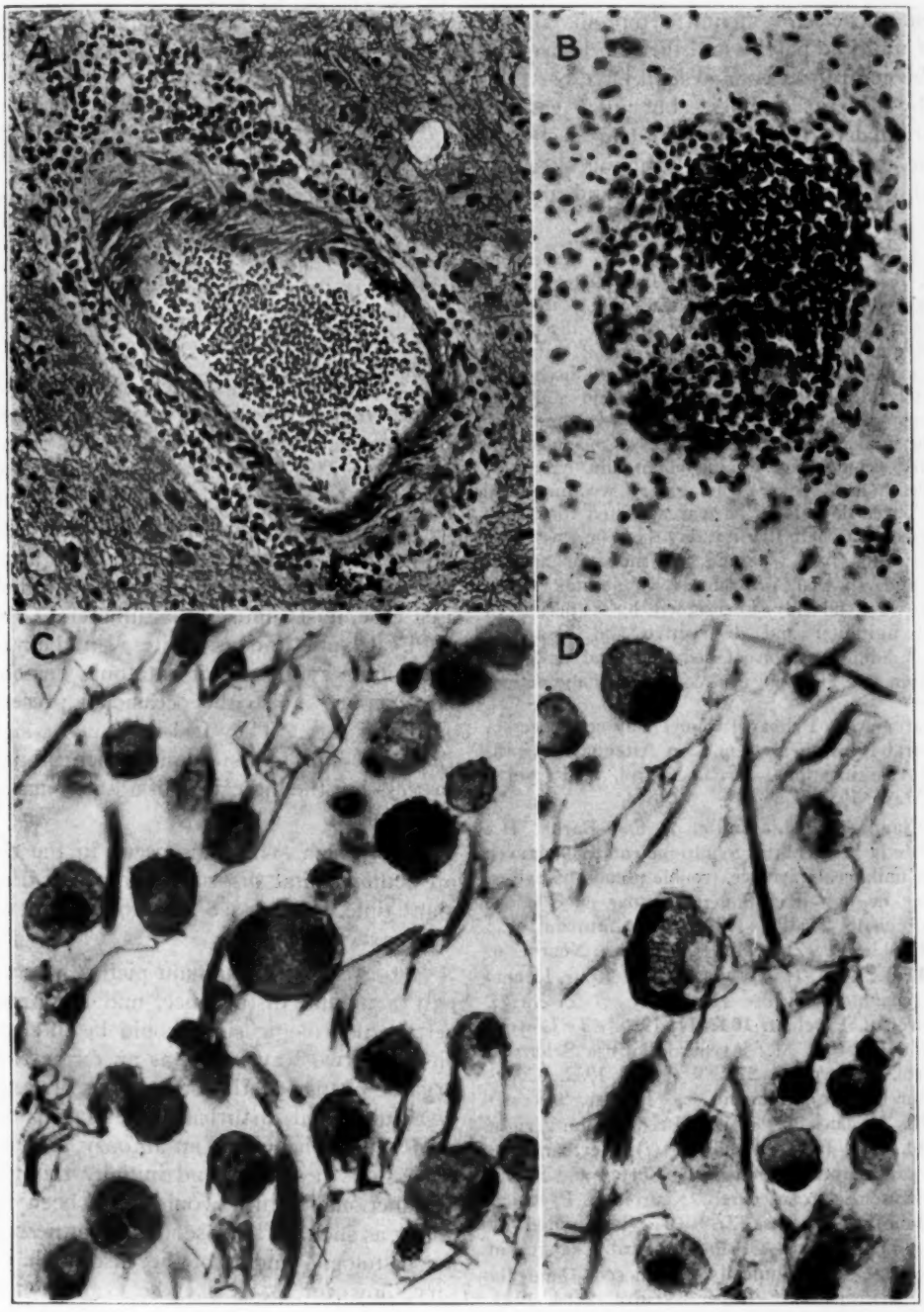

Fig. 4.—*A*, perivascular infiltration, consisting of lymphocytes, gitter cells, large mononuclear cells and some plasma cells; hematoxylin and eosin stain. *B*, perivascular granulomatous formation, composed mostly of lymphocytes and some large mononuclear elements; Nissl stain, medium power magnification. *C* and *D*, globoid cells with two, three or four nuclei; hematoxylin and eosin stain; high power magnification.

From the point of view of histologic diagnosis, in view of the type, character, distribution of the demyelinating process and duration of the disease, this condition may be considered as (1) disseminated en-

cephalomyelitis of unknown nature, or (2) acute multiple sclerosis of Marburg's and Baló's variety. We prefer to use a simple and more comprehensive term, that of a primary demyelinating disease of the central nervous system, of the acute and sporadic type, according to Ferraro's [4] classification.

A great variety of mental symptoms in the course of multiple patchy and diffuse demyelination of the central nervous system have been described by several authors,[5] but in 1 case in particular, that of Holt and Tedeschi,[6] a clinicopathologic syndrome closely resembling ours was presented. We shall recapitulate and discuss this case.

J. E., a white man aged 55, had no history of nervous or mental disease in the family. The past personal history showed nothing of importance except that the patient entered a state hospital for mental disease in 1924. There a diagnosis of dementia precox, catatonic type, was made. Five months later he was discharged as completely recovered, and he showed no abnormal mental symptoms for the next eighteen years, until the onset of the fatal illness, with restlessness and insomnia. He said that people were talking about him, expressed fears of death and spoke of imaginary weddings and funerals. Three days later he was admitted to a state psychiatric hospital. On the first day there he was found lying flat on his back; he did not move or answer questions and showed pronounced flexibilitas cerea. This state was suddenly interrupted by a period of excitement, agitation and destructive and assaultive tendencies. Administration of sedatives had no effect on the excitement. The physical condition of the patient declined rapidly; he became incontinent and untidy. During the night of the seventh day of his illness, the temperature rose to 104 F., and he became cyanotic and dyspneic. Neurologic examination at this stage of the illness as well as one made four days earlier, failed to reveal anything of significance; the blood pressure was 162 systolic and 90 diastolic; examination of the blood and all other laboratory tests gave results within normal limits. Death occurred on the morning of the eighth day of illness.

Autopsy did not reveal anything significant in the chest or the abdominal viscera. The brain was shrunken; the vessels at the base of the brain had thin walls and did not show appreciable arteriosclerotic changes. Histologic studies disclosed features "typical of a primary demyelinating process, characterized by . . . sharp demarcation and limitation of the lesions to the white substance of the brain, . . . [with] relative integrity of the overlying cortex down to and including the arcuate bundles."

COMMENT

That in the course of schizophrenia neurologic symptoms may be detected is a well established occurrence, if one wishes only to refer to the studies of Muhlig.[7] In 65 of 500 cases of schizophrenia, the author found neurologic signs, such as nystagmus, anisocoria, tremors, poor coordination, occasional dysarthria, facial asymmetry, absence of corneal and pharyngeal reflexes and, in 1 case, nystagmus and a unilateral Oppenheim sign. Claude and associates,[8] in their study of the motor syndrome of catatonic dementia precox, reported also the occasional presence of a Babinski sign. They feel that such a sign is not the expression of a systemic structural pathologic process but the indication of a functional dynamic disturbance.

When such symptoms occur in the course of an acute mental disorder leading to death in a short time, one can see the difficulty in evaluating their exact meaning.

In our case the dominant picture was undoubtedly a mental disturbance, and the presence of certain neurologic signs could be interpreted in either of two ways, i. e., as an expression of an organic change in the brain or as an expression of a functional disturbance. If our patient had died without benefit of an autopsy, all the neurologic signs described and initially thought to be of functional nature would have been recorded finally as such. The observations at necropsy and the histologic studies of the case made it necessary, however, to revise the evaluation of such symptoms, and any doubt concerning the original interpretation of the neurologic symptoms is justified.

4. Ferraro, A.: Primary Demyelinating Processes of the Central Nervous System (An Attempt at Unification and Classification), Arch. Neurol. & Psychiat. **37**:1100 (May) 1937.

5. (*a*) Claude, H.; Lhermitte, J., and Baruk, H.: Pathologie de la pré-sénilité. Syndrome catatonique avec négativisme unilateral; aphasie, trouble pseudo-bulbaires, perturbations de la nutrition générale par encéphalose diffuse, Encéphale **27**:175, 1932. (*b*) Guttmann, E.: Die diffuse Sklerose, Zentralbl. f. d. ges. Neurol. u. Psychiat. **41**:1, 1925. (*c*) Weimann, W.: Zur Kenntnis der sogenannten "diffuse Hirnsklerose," Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:411, 1926. (*d*) Löwenberg, K., and Fulstow, M.: Atypical Diffuse Sclerosis, Arch. Neurol. & Psychiat. **27**:389 (Feb.) 1932. Courtois and Borel.[2h] (*e*) Bouman, L.: Diffuse Sclerosis (Encephaliltis Periaxialis Diffusa), Bristol, John Wright & Sons, Ltd., 1934 (cases 3 and 4). (*f*) Wertham, F.: Small Foci of Demyelinization in the Cortex and Spinal Cord in Diffuse Sclerosis, Arch. Neurol. & Psychiat. **27**:1380 (June) 1932 (case 2). (*g*) Gans, cited by Bouman.[4e] (*h*) Ferraro, A.: Pathological Changes in the Brain of a Case Clinically Diagnosed Dementia Praecox, J. Neuropath. & Exper. Neurol. **2**:84, 1943. (*i*) Cardona, F.: Istologia della malattia di Schilder familiare, Riv. di pat. nerv. **54**:1, 1939 (case 1). (*j*) Roizin, L.; Helfand, M., and Moore, J.: Disseminated, Diffuse and Transitional Demyelinations of the Central Nervous System, J. Nerv. & Ment. Dis. (case 3), to be published.

6. Holt, E. K., and Tedeschi, C.: Cerebral Patchy Demyelination, J. Neuropath. & Exper. Neurol. **2**:306, 1943.

7. Muhlig, W. A.: Schizophrenia—Neurologic Signs, J. Michigan M. Soc. **39**:116, 1940.

8. Claude, H.; Baruk, H., and Thévenard, A.: Le syndrome moteur de la démence précoce catatonique, Encéphale **22**:741, 1927.

The fundamental organic cerebral process in our case was one of acute demyelination. Some authors might define the pathologic process as Schilder's disease, or encephalitis periaxialis diffusa. We prefer to call it an acute demyelinating condition, following Ferraro's [4] concept of grouping together all the demyelinating diseases, in an attempt to eliminate confusion and a variable nomenclature for the same fundamental clinicopathologic process.

What we wish to emphasize with the description of our case is the fact that organic processes of the brain may precipitate a syndrome which from the clinical standpoint is predominantly a mental one and that such a syndrome may possess all or most of the features of what clinically we consider an acute schizophrenic syndrome.

It is not our intention to build up an organic concept of schizophrenia. We wish only to focus attention on the possibility that acute mental syndromes which have all the earmarks of a so-called functional psychosis may ultimately prove to be a collection of symptoms precipitated by a definite organic disease of the brain. The need for emphasis on such an occurrence is quite evident when one considers the possibility that some of these acute schizophrenic syndromes may lead to death without the benefit of an autopsy control.

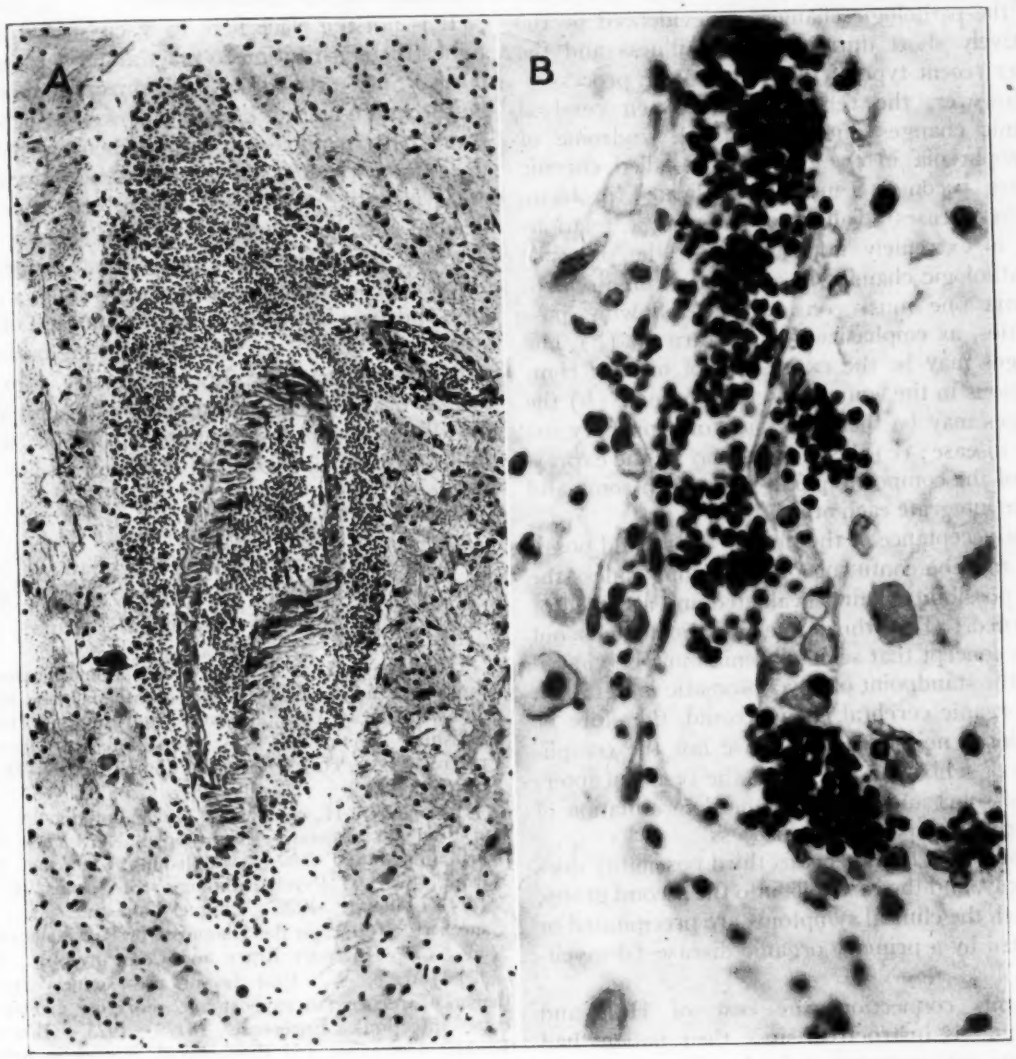

Fig. 5.—*A*, perivascular hemorrhages surrounded at its periphery with perivascular inflammatory cells; hematoxylin and eosin stain, medium power magnification. *B*, diapedesis, red blood cells in an area of demyelination; hematoxylin and eosin stain, high power magnification.

The case which we have described had definite pathologic clinical features in common with the case of an acute schizophrenic catatonic syndrome described by Holt and Tedeschi.[6] These common features are: (1) increased psychomotor activity, stereotopy, impulsiveness, bewilderment, nega-

tivism and possible hallucinations; (2) short duration of the disease and rather sudden death; (3) fleeting neurologic signs, the value of which was debatable during the patient's life, and (4) presence in the central nervous system of a process of acute demyelination.

In our case, as well as in the case of Holt and Tedeschi,[6] there seems to be no question as to the close relationship between the clinical symptoms and the pathologic changes, as evidenced by the relatively short duration of the illness and the rather recent type of the morphologic process.

However, the relationship between cerebral organic changes and the clinical syndrome of schizophrenia in the cases of so-called chronic disease becomes a more complicated problem. In these cases evaluation of such a relationship is extremely important. In the presence of pathologic changes in cases of chronic schizophrenia one must consider the following possibilities, as emphasized by Ferraro:[9] (*a*) The changes may be the expression of organic complications in the course of schizophrenia; (*b*) the changes may be the expression of a primary organic disease; (*c*) the changes may be the expression of the composite picture, in which soma and psyche integrate each other.

The acceptance of the first or the second possibility may be confusing or misleading unless the third possibility is first evaluated and accepted or discarded. This third interpretation stems out of the concept that schizophrenia must be viewed from the standpoint of psychosomatic integration. The organic cerebral change could, therefore be considered neither as the cause nor the complication of schizophrenia but as the result of interplay of soma and psyche in the determination of the structural pathologic process.

In our case, however, this third possibility does not apply, and the case falls into the second group, in which the clinical symptoms are precipitated or activated by a primary organic disease (demyelination).

In this connection, the case of Holt and Tedeschi[6] is instructive, since their patient had an acute schizophrenic episode of the catatonic type as far back as 1924, recovering from it five months later. We do not know what precipitating factors at that time determined this clinical manifestation. The occurrence of such a schizophrenic episode indicates that in their case there could have existed a constitutional predisposition to react along a schizophrenic pattern. This pattern of reaction, which in 1924 might have been precipitated by psychogenic stimuli, was produced eighteen years later by an organic disease of the brain. Such considerations emphasize the fact that in the background of our case, as well as of the case of Holt and Tedeschi, there must have been a potential tendency to react along schizophrenic lines and that irrespective of the precipitating factor, whether psychogenic or organic, the schizophrenic pattern presented itself as the dominant clinical manifestation.

It is not the place here to discuss what determines the constitution to react along certain patterns. Such a constitution in schizophrenia might be the expression of heredity, as well as of structural pattern in terms of biochemical lability or of morphology, in which the vascular[10] and vegetative systems[11] or the endocrine and general metabolic processes[12] may play a role. We feel, however, that constitutional factors are not sufficient in themselves to bring about a mental syndrome but that constitutional predisposition must be activated by precipitating factors of either psychogenic or organic nature. In our case an organic precipitating factor brought about the development of a symptom complex which clinically was diagnosed as a schizophrenic syndrome.

SUMMARY

A clinicopathologic study was made of a 34 year old woman who died after a brief, acute psychosis, presenting the clinical features of a

9. Ferraro, A.: Recent Advances and Progressive Trend of Neuropathology in Psychiatry, Psychiatric Quart., to be published.

10. Lewis, N. D. C.: The Constitutional Factors in Dementia Praecox, Nervous and Mental Disease Monograph 35, New York, Nervous and Mental Disease Publishing Company, 1923; Research in Dementia Praecox, New York, National Committee for Mental Hygiene, 1936.

11. Eppinger, H., and Hess, L.: Vagotonia (A Clinical Study in Vegetative Neurology), New York, Nervous and Mental Disease Publishing Company, 1917. Kempf, E. J.: Psychopathology, St. Louis, C. V. Mosby Company, 1920. Laignel-Lavastine, M.: The Concentric Method in the Diagnosis of Psychoneurotics, New York, Harcourt Brace and Company, Inc., 1931.

12. Mott, F. W.: Etat des organes sexuels dans la démence précoce (en rapport avec l'origine genitale de cette affection), Encéphale **18**:73, 1923. Bowman, K. M.: Endocrine and Biochemical Studies in Schizophrenia, A. Research Nerv. & Ment. Dis., Proc. **5**:262, 1928; Endocrine and Biochemical Studies in Schizophrenia, J. Nerv. & Ment. Dis. **65**:465, 1927. Whitehorn, J. C.: Effects of Glucose upon Blood Phosphates in Schizophrenia, A. Research Nerv. & Ment. Dis., Proc. **5**:257, 1928; Review of Psychiatric Progress 1942; Endocrinology, Biochemistry and Neuropathology, Am. J. Psychiat. **99**:595, 1943. Hoskins, R. G., and Sleeper, F. H.: Organic Functions in Schizophrenia, Arch. Neurol. & Psychiat. **30**:123 (July) 1933. Looney, J. M., and Freeman, H.: Volume of Blood in Normal Subjects and in Patients with Schizophrenia, ibid. **34**: 956 (Nov.) 1935. Gjessing, R.: Beiträge zur Kenntnis der Pathophysiologie periodisch katatoner Zustände: Versuch einer Ausgleichung der Funktionsstörungen, Arch. f. Psychiat. **109**:525, 1939. Ferraro.[9]

schizophrenic reaction syndrome (catatonic type). Neuropathologic studies revealed a symmetric acute demyelinating process of the central nervous system, of unknown nature.

The relationship between the clinical symptoms and the pathologic changes is emphasized not to create an organic concept of schizophrenia but merely to illustrate that a demyelinating process acting as a somatogenic factor may precipitate, in certain cases, an acute mental syndrome, which may or may not be associated with fleeting neurologic symptoms, the evaluation of which is at times difficult. The clinical characteristics of the acute mental episode may at times assume the features of a typical acute schizophrenic syndrome, and such a diagnosis might be retained throughout the life of the patient.

722 West One Hundred and Sixty-Eighth Street.

A VISUAL RETENTION TEST FOR CLINICAL USE

LIEUTENANT COMMANDER ARTHUR L. BENTON, H(S), U.S.N.R.

The visual retention test to be described here was developed as a practical means of fulfilling what I have long felt to be a need in the usual clinical examination of patients, namely, a short test to supplement the auditory-vocal digit span test in the investigation of immediate memory.

The auditory-vocal digit span test, devised in 1887 by Jacobs,[1] has become a stable feature of most clinical examination schemes. It measures retention or immediate memory, which is justifiably considered to be a significant aspect of mental capacity and one which is especially important clinically because of its close relationship to mental impairment. The test has obvious technical advantages, such as brevity of administration, lack of need for test materials and the objective character of the patient's performance.

Nevertheless, while it is a useful single test, both clinical experience and experimental observations indicate that it cannot be considered to be in itself an adequate measure of retentive capacity and that to make a global judgment concerning a patient's retentive capacity on the basis of this test alone, as is so often done, is quite unwarranted. Clinical experience shows that a poor performance on the auditory-vocal digit span test is by no means necessarily indicative of defective retentive capacity. It is well known that emotional tension can significantly impair performance on the test. Indeed, continued experience suggests that it is a test which is unusually sensitive to emotional influences. Consequently, a poor performance in a tense patient does not permit unequivocal interpretation. The poor performance might be due to emotional disturbance; yet one has no evidence that this is necessarily the case. The whole performance, therefore, must be discounted as neither indicating nor ruling out impairment in retention. Since the possibility of emotional disturbance should be considered in all instances of defective performance on the test, even when emotional tension may not be obvious, defective performance is always open to question unless it is supported by defective performances on other retention tests. In addition, one observes that a certain proportion of normal persons who exhibit no defects in the performance of other mental tasks or retention tests do poorly on this test. The reasons for these defective performances on the part of some normal subjects are not well established and can be counted only as the expression of the range of "individual differences" to be found in the measurement of any trait. Finally, the inadequacy of a single retention test like the auditory-vocal digit span is quite evident when one considers the frequently specific nature of neuropathologic disabilities. A patient's "auditory memory" may be intact at the same time that his "visual memory" is defective. His performance on a retention task involving speech as the motor response may be adequate, while the same task involving graphic activity as the motor response evokes a defective performance.

In this respect, four characteristics of the auditory-vocal digit span test which define its specific nature and which allow for "normal" variations in efficiency in respect to each characteristic should be mentioned: (1) The sensory component is auditory; (2) the motor component is vocal; (3) the material to be retained (numbers) is of a symbolic nature; (4) the test is an "interpersonal" task, involving a constant vocal exchange between patient and examiner.

Experimental psychologic investigation has indicated that when a number of retention tests are given to a group of subjects, the intercorrelations of the scores are not high enough to warrant the substitution of one test for another. Statistical analysis of test results[2] have yielded evidence for the existence of an "immediate memory factor," but as yet an adequate single test for the valid assessment of this "immediate memory factor" has not been devised. The practical implications of the experimental work on the problem are clear. In the present state of knowledge of memory functions and of mastery of

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

1. Jacobs, J.: Experiments on "Prehension," Mind **12**:75-79, 1887.

2. Thurstone, L. L.: Primary Mental Abilities, Psychometric Monograph, no. 1, Chicago, University of Chicago Press, 1938.

the technic of their measurement, one cannot depend on one test alone to give a valid index of a patient's retentive capacity.

The retention test which I have devised is a "memory for designs" test, the aim of which is to supplement the auditory-vocal digit span test as a measure of retention. In its construction certain conditions were kept in mind:

1. The test should be brief, so that it can be conveniently employed in a test battery of reasonable length. This condition is considered to have been fulfilled, since the total time required for administration is four minutes.

Visual retention test (Benton).

2. The test should involve sensorimotor components which are different from the auditory-vocal digit span test. This it does in that it utilizes vision as the sensory component and drawing as the motor component.

3. The material to be retained should be of a nonsymbolic nature. This aim is accomplished by utilizing abstract designs rather than numbers, letters, words or pictures.

4. The test should be a less "interpersonal" task than the auditory-vocal digit span test. This condition is fulfilled in that there is no necessity for conversation between patient and examiner after the initial instructions have been given. The patient does not "talk to" the examiner in giving his response but works alone, thereby making the task more impersonal than the digit span test.

5. The test should be of such a degree of difficulty that normal persons rarely do poorly on it, thereby enhancing the diagnostic value of defective performance on the test. The normative data to be presented here indicate that this condition has been fairly well fulfilled.

6. Equivalent forms of the test should be available, so that a patient may be examined with a minimum of practice effect.

DESCRIPTION OF THE TEST

The visual retention test (figure) consists of seven cards, 5 inches by 8 inches (12.7 by 20.3 cm.), on which one or more designs have been drawn in india ink. The cards are roughly graded in difficulty, the easier ones being presented first. The larger, central, figures have a maximum height and width of 2 inches (5 cm.). The smaller, peripheral, figures have a maximum height and width of 0.5 inch (1.3 cm.). Two sets (forms *A* and *B*) of seven cards each have been constructed.

Administration.—The patient is given blank sheets of paper, preferably 5 inches by 8 inches, and a pencil. He is told that he will be shown a design for ten seconds and that when it is removed he is to draw the design. A separate sheet of paper is used for each drawing. Each card is presented without comment. The patient's performance may be praised.

Scoring.—The scoring standards have been made extremely lenient, since one is interested not in the patient's drawing ability but in his capacity to retain momentarily a visual impression. Any reproduction which the examiner can consider an essentially correct reproduction, in spite of minor distortions, is counted as a success. A manual of directions, including specific scoring samples, has been written in connection with the test. My experience has been that with the aid of these scoring samples practically perfect agreement in scoring between different raters is achieved. The scoring of a single reproduction is on an "all or none" basis, being graded as adequate or inadequate. Since there are seven cards, scores may range from 0 to 7.

NORMATIVE DATA

The accompanying table shows the distribution of scores for the group of 160 subjects on whom the test was standardized. The subjects were, with a few exceptions, patients at a Naval hospital. They were almost all men, there being only 5 women in the group. The ages ranged from 17 to 51 years, the median age being 22 years. Some notion of the character of the group may be gained from the following diagnostic classification:

Distribution of Scores of One Hundred and Sixty Subjects on the Visual Retention Test

Group	No. of Subjects	Form	Score 0	1	2	3	4	5	6	7	Mean	Median
Superior.....	10	A	..	..	..	..	..	1	6	3	6.2	6
Intelligence...	14	B	..	..	..	..	1	2	7	4	6.0	6
Average.....	35	A	..	..	..	..	1	11	17	6	5.8	6
Intelligence...	35	B	..	..	..	1	1	11	14	8	5.8	6
Dull average..	10	A	..	..	..	1	..	5	3	1	5.3	5
Intelligence...	10	B	..	..	..	..	4	4	..	2	5.0	5
Borderline....	13	A	..	..	1	3	6	2	1	..	3.9	4
Intelligence...	12	B	..	..	1	3	3	4	1	..	4.1	4
Moron.....	10	A	2	..	3	2	2	1	..	..	2.5	2.5
	11	B	1	4	1	4	..	1	..	..	2.1	2

Diagnosis	No. of Patients
Normal	34
Psychoneurosis	43
Psychopathic personality	42
Mental deficiency, moron	21
Epilepsy and related states	14
Concussion and head injury	6

None of these patients showed evidence of an acquired impairment of intellectual function. In

the table, "superior" intelligence indicates an intelligence quotient of above 109; "average" intelligence, an intelligence quotient of 90 to 109; "dull average" intelligence, an intelligence quotient of 80 to 89; "borderline" intelligence, an intelligence quotient of 70 to 79, and the "moron" level, an intelligence quotient of 50 to 69, these intelligence quotient scores being computed from performance on the Wechsler-Bellevue intelligence test.

The following observations, based on inspection of the table may be made:

1. A close correlation between intelligence level and performance on the visual retention test is evident.

2. Forms A and B are practically equivalent. For the groups with superior intelligence one finds mean scores of 6, or slightly above 6, and median scores ot 6. The groups with average intelligence make mean scores slightly below 6 and median scores of 6; the groups with dull average intelligence make mean and median scores of about 5, and the groups with borderline intelligence make mean and median scores of 4. The moron groups make mean and median scores of 2.5 or below.

3. Low scores are rarely made by persons of adequate intelligence. Of the 94 subjects of average and superior intelligence, only 1 made a score as low as 3. Conversely, good scores are rarely made by persons of defective intelligence. Of the 21 subjects with mental deficiency, moron level, not a single person attained a score as high as 6.

On the basis of the normative data, the following interpretations have been assigned to the test scores:

Score	Interpretation
7	High average
6	Average
5	Low average
4	Subnormal, "borderline"
Below 4	Defective

Performances of Patients with Cerebral Lesions.—One form or the other of the visual retention test was given to a group of 16 patients who were referred for psychologic examination because of suspected mild intellectual impairment associated with an organic pathologic process and in whom positive evidence of impairment of intellectual function of varying degree was found. Of these 16 men, 2 made average scores (6); 5 made low average scores (5), and the remaining 9 made scores below the average range (4 or less). The introduction of the visual retention test into the psychologic examination served a useful purpose in defining the extent and the degree of the impairment. In these cases, the auditory-vocal digit span test, because of its sensitivity to tensional and emotional influences, frequently gave results which were of equivocal interpretive value. These officers and men, most of whom were career men and eager to remain in the Naval service and none of whom showed obvious impairment, typically evinced an attitude of considerable anxiety in their intense desire to do well on the mental tests. On the auditory-vocal digit span test, as on other tests, their postural set tended to be one of marked "concentration" and tension. This attitude, which might possibly facilitate performance on some mental tests, is certainly not conducive to good performance on the digit span test, which requires for optimal performance a certain degree of relaxation and a receptive attitude on the part of the subject. On the other hand, performance on the visual retention test, being relatively insensitive to emotional influences, could be interpreted much more readily. As the normative data show, poor performance on the part of subjects with unimpaired intellectual function is rare. Consequently, a poor performance on the visual retention test, in combination with a poor performance on the digit span test, served to establish the conclusion that a defect in retention of considerable scope did in fact exist, a conclusion which could not justifiably be made on the basis of the digit span performance alone. The combination of a good performance on the visual retention test and a poor performance on the digit span test served to indicate that at least a general defect in retention was not present. If, on the basis of general observation of the patient and of other test performances, the examiner was inclined to doubt the validity of the results of the digit span test, the adequate performance on the visual retention test would support the impression that the retentive capacity of the patient was unimpaired. The combination of a poor performance on the visual retention test and a good performance on the digit span test would indicate that visual retention alone was defective, a type of impairment not infrequently encountered in patients with cerebral lesions. Finally, the combination of adequate performances on the two tests would definitely establish the absence of an immediate memory defect.

In summary, it can be reported that a majority of patients suffering from mild impairment of intellectual function on an organic basis can be expected to show subnormal efficiency on the visual retention test and that the test has shown

itself to be of value in defining the scope of the impairment and in complementing the performance on the digit span test.

REPORT OF CASES ILLUSTRATING USE OF VISUAL RETENTION TEST [3]

CASE 1.—Application of the visual retention test in the case of a 26 year old Marine recovering from a shrapnel wound in the left parietal area may be noted to indicate how the test can aid in arriving at a judgment concerning the mentality of a patient with a language disorder. At the time of examination the patient no longer showed an overt speech disturbance, although previously he had shown marked anomia and "word-finding" disturbance. At this time he showed an incomplete homonymous hemianopsia, which was rapidly clearing, pronounced acalculia (but no finger agnosia or right-left disorientation) and impairment in reading and writing. His reading was slow, labored and fatiguing. He could not write to dictation but could copy written material. Performance on information and vocabulary tests was average and indicated that the pretraumatic intellectual level had been average, a conclusion in accord with his educational and social history. On the digit span test, he could repeat only 4 digits and reverse only 3 digits. On an "object memory" test, involving the verbal recall of objects which had been exposed to him, his performance was also notably defective. On the basis of the results of these two tests alone one might have concluded that "retentive capacity in general" was considerably impaired and that his mental disabilities extended beyond the language sphere. However, on the visual retention test he made a score of 5, corresponding to a low average performance. Thus, given a retention task in which speech was not involved as the motor element in response, his performance was fairly adequate, a fact which had obvious bearing on the question of whether intellectual impairment was present in addition to the disturbance in the formation, expression and utilization of symbols.

In addition, the results clearly suggested that, although the overt speech disorders (anomia, word-finding disturbance) were no longer apparent, a language disturbance was still present. This, and not defective "basic retentive capacity," appeared to account for the poor performance on the two retention tests involving speech as the motor element in response and symbols as the content of the response. In view of the marked agraphia, the adequate performance on the visual retention test is especially noteworthy.

CASE 2.—A pharmacist's mate, aged 20, sustained a bullet wound in the left frontoparietal region, with immediate flaccid paralysis of the right arm and both legs and complete expressive aphasia for twenty-one days. At the time of psychologic examination, approximately three and a half months after his injury, he showed a spastic right hemiparesis, the paralysis being more severe in the arm than in the leg or face. No sensory disturbances or hemianopsia was present. There was some residual aphasia in the form of hesitant speech and occasional blocking but no receptive aphasia or anomia. Psychologic examination indicated superior pretraumatic intelligence. Performance on tests of arithmetical reasoning and calculation was extremely unstable. One minute the simplest calculation could not be made, and a few minutes later much more difficult calculations would be done readily. Abstract reasoning ability was unimpaired. On the digit span test he could repeat only 5 digits and reverse only 3 digits. On an object memory test, involving the verbal recall of representations of objects seen, performance was defective. However, on the visual retention test, in drawing with the left hand, performance was average (score 6). Two aspects of the performance are noteworthy: 1. As in case 1, the language disturbance evidently led to disturbed performance on retention tests involving speech and containing symbolic material, such as the digit span and the object memory test. The visual retention test, involving drawing as the motor response and containing nonsymbolic material, was done well, indicating the limitation of his defects to the language sphere. 2. Despite the motor defect and the necessity for drawing with the left hand, performance on the visual retention test was adequate, indicating that the scoring standards are sufficiently lenient to insure that the test is in no sense one of drawing ability.

Performances of Patients with Severe Mental Disorder.—In this group of 17 patients were included psychotic patients showing impairment of intellectual function, disturbed psychopaths and 2 patients with hysterical pseudodementia associated with amnesia. Performance on the visual retention test was typically poor, only 1 patient achieving an average score (6), 2 patients making a low average score (5) and the rest making scores of 4 or less. The digit span performance of these patients, likewise, tended to be poor.

Performance of Older Subjects.—The question whether there is a decline in performance on the visual retention test on the part of older persons has not been systematically studied. Within the age range (17 to 51 years) of the normative group, inspection of the data shows no decline in efficiency with age. To what extent persons in the fifties and sixties would show a decline in efficiency must remain an open question until an adequate sample of that population is investigated. My expectation, based on what is known about the "normal" decline of retentive ability with age, is that persons in the 51 to 60 year age group would show a slight decline in test performance and that persons over 60 years of age would show a more pronounced loss in retentive ability.

Sex Differences in Performance.—This question has not been investigated, since the normative group was predominantly male. The 5 women of the group were of either average or superior intelligence, and all made scores within the average range. Significant sex differences in performance on the test are not expected, but this question should be systematically studied.

3. The 2 patients whose cases are reported here are not included in the group of 16 persons with cerebral lesions discussed in the preceding section.

SUMMARY

A brief test of visual retentive capacity, available in two equivalent forms, has been developed for use in the mental examination of patients as a supplement to the auditory-vocal digit span test.

The test involves sensorimotor components which are different from those involved in performance on the digit span test; the material to be retained is of a nonsymbolic nature, and performance on the test is relatively insensitive to emotional and tensional influences.

The normative data indicate a close relationship between the visual retention test score and the level of general intelligence.

Investigation of the performances of patients with cerebral lesions indicates that the test is of value in defining the scope and severity of intellectual impairment.

Normative scores have been developed on the basis of the standardization data, and a manual of directions for administration and interpretation of the test has been developed.[4]

4. The test materials and a manual of directions for constructing, administering and scoring the test are available on request to Dr. A. L. Benton, Student Personnel Bureau, College of the City of New York, Convent Avenue and One Hundred and Fortieth Street, New York.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

STUDIES ON PALMAR SWEATING. JACOB J. SILVERMAN and VERNON E. POWELL, Am. J. M. Sc. **208**:297 (Sept.) 1944.

Silverman and Powell used a colorimetric technic for measuring sweating of the palms and finger tips. The technic had the advantages of availability, economy, objectivity, practicability and permanence. It consisted in the use of a liberal amount of ferric chloride (25 per cent solution), applied to the area with an ordinary cotton-tipped wooden applicator. The area was then dried thoroughly and contact was maintained for exactly three minutes with a chemically treated paper (5 per cent solution of tannic acid). The tannic acid reacted with iron to form a stain on the paper varying from gray-blue to blue-black. The results are graded from 0, or a faint response, to 3, or an intense response. Palmar sweating is considered under the headings of thermoregulatory, excretory, chemical, axillary, gustatory, spinal reflex and emotional. The authors believe that the palm is one of the few places where emotional sweating takes place and is an indicator of emotional disturbances. Of over 1,100 patients, approximately 25 per cent showed a grade 3 response, and over 80 per cent showed a combined grade 2 and 3 response. Those patients who showed a grade 3, or intense, response revealed evidence of emotional strain or a disturbance of the autonomic nervous system. MICHAELS, M. C., A. U. S.

THE EFFECTS OF ACETYL-BETA-METHYLCHOLINE IN HUMAN SUBJECTS WITH LOCALIZED LESIONS OF THE CENTRAL NERVOUS SYSTEM. STUART M. FISHER and GEORGE W. STAVRAKY, Am. J. M. Sc. **208**:371 (Sept.) 1944.

Fisher and Stavraky studied the effect of the administration of a suitable choline ester to human subjects with localized lesions of the central nervous system. The best results were obtained with intramuscular injections of acetyl-beta-methylcholine chloride. The effects of mecholyl chloride were studied in 12 male patients with lesions of the rostral portion of the cerebral hemisphere or with signs of involvement of the upper motor neurons. Injections of 8 to 25 mg. of mecholyl chloride dissolved in 0.3 to 1 cc. of distilled water were made into the deltoid muscle and were repeated in each patient at least on two or three occasions. Within twenty to thirty seconds after the injection of 8 to 10 mg. of mecholyl chloride normal males experienced a sensation of heat in the face. In 11 patients with lesions of the frontal lobe with or without involvement of the motor cortex, the injection of mecholyl produced an asymmetric response. During the reaction the contralateral extremities were notably colder than the ipsilateral limbs. In cases in which the lesions extended to the motor or premotor cortex, muscular tremors, slight involuntary movements, an increase in spasticity, pronounced hyperreflexia, clonus of the wrist, ankle and patella, and prominence of pathologic reflexes on the opposite side of the body characterized the later stages of the reaction. These effects of mecholyl are interpreted as resulting from a selective sensitization to chemical stimulating agents of partially isolated nerve cells situated in the chains of descending neurons of the brain and spinal cord.

MICHAELS, M. C., A. U. S.

THE INCIDENCE OF BROMISM AT WARREN STATE HOSPITAL. A. ARNOLD KIPPEN, J. Nerv. & Ment. Dis. **99**:968 (Feb.) 1944.

Kippen reviews the literature on the incidence of bromide intoxication in patients admitted to psychiatric hospitals. At the Warren State Hospital bromide determinations were carried out according to the method of Katzenelbogen and Czarski on 1,000 consecutive patients. In 12.3 per cent the level of bromides in the serum was 25 to 400 mg. per hundred cubic centimeters, whereas in 2.6 per cent the bromide level was in the "toxic range" of over 150 mg. per hundred cubic centimeters. Bromide psychoses were present in about one third of the patients with bromide levels in the "toxic range," a total incidence of 0.8 per cent of the series. CHODOFF, Langley Field, Va.

A NOTE ON THE TWO COMPONENTS OF THE DORSAL ROOT POTENTIAL. F. T. DUN and T. P. FENG, J. Neurophysiol. **7**:327 (Nov.) 1944.

Dun and Feng studied the electric potential obtained from one dorsal root in response to the stimulation of another, and distant, dorsal root. The potential was divisible into two parts: The first was unaffected by strychnine but was abolished by section of the dorsal columns between the stimulating and the recording root, and the second was strengthened by strychnine and not affected by section of the dorsal columns. Dun and Feng conclude that the second component is mediated by a number of internuncial neurons.

FORSTER, Philadelphia.

RECEIVING AREAS OF THE TACTILE, AUDITORY AND VISUAL SYSTEMS IN THE CEREBELLUM. RAY S. SNIDER and AVERILL STOWELL, J. Neurophysiol. **7**: 331 (Nov.) 1944.

Snider and Stowell studied the electrical activity of the cerebellum of the cat and monkey and the alterations in this activity produced by tactile, auditory and visual stimuli. Distinct areas were found for the reception of impulses of each modality. Tactile impulses were received (*a*) from the ipsilateral half of the body in the lateral half of the anterior lobe and in adjacent folia and (*b*) from the forefoot and hindfoot of each side in both paramedian lobules, the forefoot having a stronger contralateral representation than the hindfoot. In the anterior lobe and adjacent folia there was an anatomic localization with regional representation. The auditory area was restricted to the lobulus simplex and the tuber vermis. Decerebration failed to affect the auditory responses, but they were abolished by section of the eighth nerve and by destruction of the cochlea or the inferior colliculus. The visual area overlaps the auditory, and the pathways for the visual

responses probably involve the superior colliculus. Full anesthetic doses of sodium pentobarbital did not affect tactile responses but depressed auditory and abolished visual responses. The authors suggest that cerebellar functions are influenced by tactile, auditory and visual stimuli, as well as by impulses from proprioceptors and from the cerebral cortex.

FORSTER, Philadelphia.

SPREADING DEPRESSION OF ACTIVITY IN THE CEREBRAL CORTEX. A. A. P. LEAO, J. Neurophysiol. **7**:359 (Nov.) 1944.

Leao studied the depression of the electrical activity of the cortex of the rabbit under dial anesthesia. The depression resulted from stimulation with a tetanizing current or from mechanical stimulation and spread slowly from the area of stimulation, in all directions, to involve almost the entire cortex. Its development in any one area was gradual, and electrical activity might return to normal in the area of stimulation while distant cortical areas were still in the state of depression. Some regional variations were encountered; thus, stimulation near the occipital pole gave less consistent results than other areas. Electrical stimulation too weak to produce after-discharge produced depression. Two waves of depression could be started simultaneously in distant cortical areas. Treatment of the cortex with cocaine and section or coagulation of the cortex prevented the spread of depression beyond this region. The electrical activity of the opposite hemisphere was also depressed, and the depression of the contralateral hemisphere had its inception at a region symmetric with the stimulated area. Somatic sensory and optic responses were decreased during the depression of the electrical activity of the appropriate area. Motor responses to stimulation were decreased during depression of the electrical activity of the motor area. During depression of the electrical activity of one hemisphere depression of the electrical activity of that hemisphere was also obtained by stimulation of the opposite hemisphere. During the depression of the electrical activity strong repetitive electrical stimuli failed to produce self-continuing electrical responses. The electrical activity due to application of strychnine or acetylcholine could likewise be depressed. During the periods of depression of the electroencephalogram electrical activity differing from the spontaneous activity was frequently observed. This consisted of large, slow negative waves; rapid, spikelike potentials, or activity similar to the tonic-clonic responses of experimental epilepsy. Leao stresses the close relation between the spreading depression and the electrical discharges of experimental epilepsy and indicates that both are probably mediated by the same cortical elements and both are mainly or exclusively cortical.

FORSTER, Philadelphia.

PARALYSIS WITH HYPOTONICITY AND HYPERREFLEXIA SUBSEQUENT TO SECTION OF BASIS PEDUNCULI IN MONKEYS. B. W. CANNON, H. W. MAGOUN and W. F. WINDLE, J. Neurophysiol **7**:425 (Nov.) 1944.

Cannon, Magoun and Windle studied 6 monkeys in whom the right or the left basis pedunculi had been sectioned. The result was a paralysis intermediate between spastic paralysis and hypotonic paresis. They found hypotonicity of all muscle groups except the extensors of the digits, hyperactive deep reflexes and absence of clonus. They conclude that inhibitory pathways descending from the cortex do not all course entirely within the basis pedunculi. The fibers concerned with hypertonicity and clonus have for the most part deviated from the corticospinal projection prior to reaching the cerebral peduncle, whereas the fibers whose interruption leads to hyperreflexia accompany the corticospinal projection in the cerebral peduncle but deviate before reaching the pyramids.

FORSTER, Philadelphia.

THE DEFECT IN UTILIZATION OF TOCOPHEROL IN PROGRESSIVE MUSCULAR DYSTROPHY. ADE T. MILHORAT and W. E. BARTELS, Science **101**:93 (Jan. 26) 1945.

Milhorat and Bartels present a preliminary report on observations on 15 patients with progressive muscular dystrophy. They report that tocopherol (either the free substance or the acetate, phosphate and succinate esters) administered orally was without effect on the creatinuria of their patients except in 1, in whom the dystrophic process was of unusually slow progression. However, tocopherol that had been incubated in the stomach of a normal man lowered the creatine output of about one-half the subjects. A number of other experiments are mentioned, and on the basis of their results and of observations by other workers, the authors postulate requirements for the substance with which tocopherol forms a condensation product in the body. Inositol is one substance which seems to satisfy these requirements. A water-soluble condensation product was prepared by refluxing benzene hexachloride and alpha tocopherol in absolute alcohol containing potassium hydroxide.

Further observations suggest that tocopherol forms a condensation product with inositol in the gastrointestinal tract (tocopherol-inositol ether) and that the defect in muscular dystrophy is a deficiency in the reaction of condensation. The degree of this deficiency appears to determine the rapidity with which muscular disability progresses. Patients in whom the disease process is mild can synthesize sufficient amounts of the condensation product when large amounts of both tocopherol and inositol are given together, but patients in whom the disease is more rapidly progressive will probably require the condensation product itself.

GUTTMAN, Philadelphia.

EXPERIMENTAL EDEMA OF THE BRAIN: I. METHODS OF PRODUCING EDEMA OF THE BRAIN. S. OBRADOR and J. PI-SUÑER, Bol. d. Lab. de estud. med. y biol. **1**:37 (April) 1942.

Obrador and Pi-Suñer used the method of Le Beau and Bonvallet to produce acute edema of the brain. The brain stem was sectioned in the region of the fourth ventricle in adult dogs anesthetized with pentobarbital sodium. Trephine openings in both parietal regions were covered by observation windows. Lesions other than section in the region of the floor of the fourth ventricle also produced pronounced swelling of the cerebral hemispheres. Lesions in the floor of the fourth ventricle causing arterial hypertension were most likely to give rise to cerebral edema. During the experiments it was usually found that the cerebral edema was preceded by a rise in blood pressure. A rise in blood pressure following injury to the floor of the fourth ventricle was not always followed by cerebral edema. Compression of the region of the fourth ventricle usually caused transitory cerebral edema. The edema of the brain was more lasting in almost all the cases than

the rise in blood pressure. Transections in the region of the fourth ventricle caused a more persistent cerebral edema than other lesions in the same region.

SAVITSKY, New York.

Neuropathology

ENCEPHALITIS AFFECTING THE BASAL GANGLIA IN MONKEYS. RICHARD B. RICHTER, J. Neuropath. & Exper. Neurol. **4**:16 (Jan.) 1945.

Richter reports the pathologic observations in 2 monkeys (Macaca mulatta) with acute encephalitis of unknown origin, presumably spontaneous. One of the animals manifested involuntary movements of choreiform type. Histologic study revealed the presence of focal, bilateral necrotizing lesions confined to the corpus striatum and the globus pallidus. The appearance of chorea in 1 of the monkeys demonstrates that it may occur in the monkey in the presence of bilateral damage to the basal ganglia with an otherwise intact nervous system.

GUTTMAN, Philadelphia.

PORENCEPHALY: II. STUDIES IN PHLEBOTHROMBOSIS AND PHLEBOSTASIS. OTTO MARBURG, P. R. REZEK and M. B. MARKS, J. Neuropath. & Exper. Neurol. **4**:43 (Jan.) 1945.

Marburg, Rezek and Marks report the case of an infant who was delivered by forceps, with bleeding from the left ear and ecchymoses over the body. After a small blood transfusion the bleeding ceased. The clot retraction time was greatly prolonged. At the age of 4 months the child had difficulty with vision, horizontal nystagmus and bilateral optic nerve atrophy. Hydrocephalus was present. At 10 months puncture of a fontanel was performed, which was followed by a septic temperature. Death occurred several days later. A porencephalic cyst was found at autopsy.

The authors conclude that the pathologic process underlying porencephaly is a vascular hemorrhage, thrombosis or stasis in the areas of drainage of the vena magna Galeni or of some cortical veins. The important factor in the pathogenesis is the association of the vascular process with hydrocephalus.

If inflammation causes porencephaly, it does so exclusively through obstruction of the veins, and polioencephalitis does not play a role. Arrested development probably does not cause porencephaly, since the changes considered as evidence of developmental disturbances may be ascribed to venous lesions.

The principal cause of the pathologic changes is trauma: injuries during delivery, particularly instrumental delivery; injury to the fetus by trauma sustained by the mother; injury to the skull shortly before or after birth. Changes in constituents of the blood, although not proved, may serve as a contributing factor.

GUTTMAN, Philadelphia.

CEREBRAL THROMBO-ANGIITIS OBLITERANS AND ITS RELATION TO PERIARTERITIS NODOSA. I. MARK SCHEINKER, J. Neuropath. & Exper. Neurol. **4**:77 (Jan.) 1945.

Scheinker reports 2 representative cases of cerebral thromboangiitis obliterans and 6 cases of periarteritis nodosa. There is a difference of opinion regarding the relation between thromboangiitis obliterans and periarteritis nodosa. Some investigators assume a close connection between the two vascular processes while others do not.

The author states the significant difference between the two conditions as follows: In thromboangiitis obliterans there is a massive proliferation of the subendothelial connective tissue, with consequent narrowing or occlusion of the vascular lumen. In periarteritis nodosa minimal secondary intimal proliferation may be observed, and then only occasionally in the final stage of the disease, when it is always associated with periarteritis. In thromboangiitis obliterans the proliferative changes are never, or are seldom, complicated by inflammatory or advanced necrotic changes. Severe inflammatory changes of the entire vascular wall, associated with necrosis of the subendothelial connective tissue and the adjacent media, are the primary and the most characteristic lesions of periarteritis nodosa. Marked degeneration of the internal elastic membrane, represented by disruption and splitting of fibers with eventual complete necrosis, is frequently observed with periarteritis nodosa, but is seldom seen with thromboangiitis obliterans. In periarteritis nodosa the pathologic changes involve the entire vascular wall; in thromboangiitis obliterans the lesions are usually confined to its inner layer. The frequently observed intramural hemorrhages in the early stage of thromboangiitis obliterans are not seen with periarteritis nodosa.

Scheinker offers the hypothesis that the characteristic early lesions of thromboangiitis obliterans may be reversible circulatory disturbances (angiospasm and vasoparalysis), which may become irreversible if of prolonged duration or repeated occurrence. The view is expressed that each of these vascular diseases has a characteristic morphology and that pathologically they should be considered as different vascular syndromes.

GUTTMAN, Philadelphia.

A REVIEW OF SOME RECENT OBSERVATIONS ON DEMYELINATION. E. WESTON HURST, Brain **67**:103, 1944.

Hurst reviews the developments in the understanding of the process of demyelination, considering them under the various hypotheses regarding the causation of demyelination. He considers in detail the evidence for the role of vascular blocking in the causation of demyelination and points out that demyelination with degeneration of axis-cylinders may result from a relatively minor obstruction of the circulation in the white matter without progression to complete necrosis. While obstructing plugs in experimental procedures may disappear rapidly after resulting in a lesion, there is no present evidence that the same factor may be present in the human brain. In reviewing the observations on the effects on the brain of chemically induced anoxia, Hurst concludes that the anoxia may be followed, according to its severity and duration, by cerebral lesions varying from cortical necrosis to demyelination of the white matter. The cortex has a greater need for oxygen, while the white matter has less recuperative power, so that a single period of less intense anoxia or a repetition of minor insults may lead to severe involvement of the white matter. As to the production of demyelination by the action of antibodies on brain tissue, Hurst reviews the work of Ferraro and Jervis and their successful production of demyelination in monkeys by this method. Hurst was unable to produce this process in other species. He points out the paucity of experimental evidence pointing to an allergic basis for demyelination. He attempted, unsuccessfully, to induce demyelination in animals with egg albumin but concludes that further study is neces-

sary to evaluate the role of antigen-antibody reactions and the responses of antibodies to brain tissue. The author points out that in the distemper of dogs the virus may be responsible for demyelination. Biochemical studies in the demyelinating diseases have been concerned with the myelolytic effect of plasma, serum or urine in vitro on the spinal cord of animals or the demonstration of various abnormal enzymes in the serum.

Hurst notes the wide diversity of agents which produced demyelination experimentally and the association between necrosis and demyelination in the same case or the replacement of demyelination by necrosis with an increase in the intensity of the pathologic agent. He concludes that demyelination is the response of the white matter to injuries short of lethal and suggests that attempts to find a single causative agent for demyelination will be unprofitable.

FORSTER, Philadelphia.

CHANGES IN THE BRAIN IN ALCOHOLIC PSYCHOSES. D. NIETO, Bol. d. Lab. de estud. med. y biol. **1**:57 (May) 1942.

Nieto reports unusual histopathologic changes in 2 adults who died during attacks of delirium tremens. No other cause for death was found. A marked increase in oligodendroglia was found in the subependymal and periaqueductal regions and about the third ventricle. In the surrounding area there was evident gliosis. The changes in the frontal regions were similar to those encountered in 6 cases of psychosis with pellagra. The subependymal proliferation of oligodendroglia is considered a reaction to toxins which appear in the spinal fluid during the course of delirium tremens.

SAVITSKY, New York.

Psychiatry and Psychopathology

INTELLECTUAL IMPAIRMENT IN HEAD INJURIES. JURGEN RUESCH, Am. J. Psychiat. **100**:480 (Jan.) 1944.

Ruesch studied the frequency and nature of intellectual impairment following head injuries. The following psychometric tests were found to be most efficacious in measuring the impairment: 100-7 test, pictorial absurdities, hole in the board test, pictorial discrimination, naming of colors and reading. The primary deficits were found to be in speed, judgment and ability to maintain sustained effort. These defects were evaluated in two ways: (1) by comparison of performance with estimated intelligence and (2) by improvement on repeated examinations.

Ruesch found intellectual impairment of slight degree in approximately one half of all subjects with head injury. With the passage of time these defects decreased in severity. Reversible impairments usually did not persist more than three months. The degree of mental impairment could be correlated to some extent with the degree of organic cerebral damage.

FORSTER, Philadelphia.

THE PSYCHONEUROSES OF WAR. J. L. HENDERSON and MERRILL MOORE, New England J. Med. **230**: 273 (March 9) 1944.

Henderson and Moore analyze a series of 200 cases of neuropsychiatric disorders in patients admitted to a military hospital in the South Pacific. They report that about 23 per cent of all patients admitted to hospitals presented neuropsychiatric problems. In 49 per cent of this number, the disorder was diagnosed as anxiety neurosis; in 20 per cent, as hysteria; in 7 per cent, as constitutional psychopathic state; in 6 per cent, as schizophrenia; in 5 per cent, as manic-depressive psychosis; in 4 per cent, as epilepsy, and in 9 per cent, as miscellaneous disorders. Almost all patients reported having a broken home or neurotic parents. Thirty per cent gave a positive history of head injury prior to induction. Thirty-five per cent had previously experienced a sudden or overwhelming trauma, such as an automobile accident. Of the last group, many had lost consciousness and suffered amnesia, as well as hysteria. These reactions recurred during bombings and shellings.

Loss of weight in the battle zone averaged roughly 21 pounds (9.5 Kg.) per patient, and polyneuritis, probably due to vitamin deficiency, was present in a number of patients. Twenty-five per cent of the patients had malaria, and 12 per cent suffered from organic cerebral damage resulting from bomb or shell blast.

Fatigue and the intensity, as well as the repetition, of traumatic experiences in the combat zone enhanced the psychoneurotic state. Those who "broke" earliest had the poorest prognosis. The chief predisposing factor was the neurotic makeup of the patient. Nightmares were an almost universal symptom in the group and were associated with concomitant reactions of the sympathetic nervous system. The nightmares usually were repetitive dreams of combat. The patients recounted these dreams to each other, apparently for catharsis, and derived some relief therefrom.

Bombing and shelling precipitated neuroses. The experience of hiding in a foxhole or other shelter subjected to enemy attack without being able to fire back was particularly unbearable, since no release from tension could be afforded by physical activity. This enforced passivity resulted in physical, as well as mental, symptoms and often recurred as the characteristic nightmare pattern.

Many of the patients were found to have had a mutually overdependent relationship with their parents. Their resultant inability to express normal hostility proved a serious handicap in the battle situation. There were frequently overidentification with the mother and fear of an abusive father.

Limitations of time restricted attempts at therapy. Sedation was the quickest approach for the relief of surface symptoms. Some occupational therapy was tried, with success. Hypnosis was also useful. In addition group psychotherapy was employed, with the therapeutist giving a necessarily superficial explanation of symptoms, as well as encouragement. The authors believe, however, that the only lasting therapy is of the individual type, although this was not practicable in the war situation.

GUTTMAN, Philadelphia.

SUBLIMATION. GÉZA RÓHEIM, Psychoanalyt. Quart. **12**:338, 1943.

Róheim believes that sublimation has three associated sources. A neurosis is the repetition of an infantile tragedy, while sublimation is the repetition of a happy infantile situation, of a traumatic situation that has been mastered successfully. In a neurosis the conflict between the superego and the ego ends in defeat of the latter. The ego pleads guilty and enters a state of perpetual mourning. The basic element of a neurosis is melancholia. In sublimation and cultural activity the ego, allied with the id, is victorious and controls the

superego. The basic element is mania. A third source of sublimation lies in the process of growth, which decreases the initial helplessness of infancy and forms the basis of the ego. Here ego and id are acting in harmony, and the superego is absent. Sublimation is a sublimation of the erotic drive and is a substitute for coition or some other type of libidinal activity. A sublimation is always based on an infantile erotic activity or fantasy. Although the superego always represses the id strivings in sublimation the id strivings reconquer the ground in a disguised form.

The neurotic part of the personality is the past; the maturation or stimulus reaction part is the present. Sublimation, although based on the past, stands for the future, or the assurance of a future of "Paradise Regained."

PEARSON, Philadelphia.

Meninges and Blood Vessels

ACUTE MENINGOCOCCAL ENCEPHALOMYELITIS. WILLIAM B. WARTMAN and IRWIN C. HANGER, Am. J. M. Sc. **208**:234 (Aug.) 1944.

Wartman and Hanger report the case of a white man aged 27 who was admitted to the hospital complaining of headache, backache and fever, which had been steadily increasing for twenty-four hours. The temperature was 101 F., and the pulse rate was 116 per minute. There was questionable stiffness of the neck, which at the time was attributed to the severe headache. Three days after admission he became irrational and was given 10 cc. of paraldehyde intravenously. The spinal fluid was grossly purulent and contained 54,900 leukocytes, mostly neutrophils, per cubic millimeter. After a stormy course, the patient died, four days after admission. The clinical diagnosis was acute cerebrospinal meningitis due to meningococcus and bronchopneumonia involving the lower lobe of each lung, of undetermined cause. Study of the central nervous system revealed a delicate film of creamy yellow pus which occupied the sylvian fissure and the sulci on the lateral and superior aspects of the brain. The dura mater was hyperemic. The cerebral hemispheres were greatly swollen. Numerous clusters of bright red, punctate hemorrhages were scattered throughout the white matter, but the gray matter was mostly spared. The tissues were extremely edematous and hyperemic, with wet, boggy, pink cut surfaces. Throughout the white matter of the entire spinal cord were numerous small hemorrhages, similar to those in the brain. All parts of the lungs were extensively consolidated, except for a few small foci at the apex and along the lower margin of the upper lobes. The microscopic examination revealed hemorrhagic, as well as inflammatory, lesions throughout the white matter of both cerebral hemispheres. They were most common in the posterior frontal, parietal and anterior occipital regions. Although clinically the condition was thought to be meningococcic cerebrospinal meningitis, autopsy revealed acute encephalomyelitis, violent and extensive, with but comparatively little meningitis.

MICHAELS, M.C., A.U.S.

MENINGOCOCCIC MENINGITIS IN SANTIAGO, CHILE, 1941 TO 1943: AN EPIDEMIC OF 4,464 CASES. ABRAHAM HORWITZ and JOSE PERRONI, Arch. Int. Med. **74**:365 (Nov.) 1944.

Horwitz and Perroni report that an epidemic of meningococcic meningitis started in the port of Valparaiso in June 1941 and extended from there until it reached Santiago, a distance of about 80 miles, three months later. The total number of cases recorded in Santiago from September 1941 to July 3, 1943 was 4,464. The incidence was approximately 1 case per 300 inhabitants, and the largest number of cases occurred in 1942. The disease was slightly more common in males than in females and was more fatal in infancy and old age than in the other periods of life. The fatality rate for all patients was 16.5 per cent; for infants under 4 years it was 28 per cent.

In a series of 450 unselected patients treated with sulfonamide compounds, the mortality was 9.3 per cent with sulfadiazine therapy, 10.7 per cent with sulfathiazole therapy and 13.3 per cent with sulfanilamide therapy. Toxic reactions occurred in 33 per cent of patients who received sulfanilamide and in 4.4 per cent of the patients who were given sulfadiazine.

GUTTMAN, Philadelphia.

MENINGOCOCCAL MENINGITIS AND MENINGOCOCCEMIA IN CHILDHOOD: A STATISTICAL STUDY OF SEVENTY-TWO CASES. JOSEPH OSBORNE, WILLIAM H. ARNONE and GEORGE I. LYTHCOTT, New England J. Med. **231**:868 (Dec. 28) 1944.

Osborne, Arnone and Lythcott report observations on 72 children, all under 12 years of age, who were treated for meningococcic meningitis or meningococcemia.

The onset was acute in 59 per cent of the cases and was ushered in by nausea and vomiting in 64 per cent, by headache in 31 per cent, by stiff neck in 17 per cent, and by a cutaneous rash and drowsiness in 14 per cent. The lesions of the skin were a valuable aid in the diagnosis of meningococcemia and were present in 82 per cent of the cases at the time of admission. The other chief complaints were as follows: convulsions, 11 per cent; fever, 10 per cent; delirium, 10 per cent; abdominal pain, 6 per cent; arthralgia, 3 per cent; myalgia, 4 per cent, and coma, 3 per cent. Convulsions were limited almost entirely to patients under 3 years of age. They occurred in 10 of the 14 children 1 year of age, in 4 of the 12 children 2 years of age and in 2 of the children 7 years old. Of the patients over the age of 3 only 1 had a convulsion.

The predominant type of organism was a type 1 meningococcus, occurring in 76 per cent of the cases in which the cultures were positive. All the patients were treated with sulfadiazine.

The most frequent complication was arthritis, occurring in 12 per cent of the cases. This was a periarthritis without active suppuration within the joint. The average time for the appearance of manifestations in the joints was six days after the onset of the disease. The symptoms persisted for about eight days. The treatment was immobilization, followed by passive motion and physical therapy as soon as the active inflammation subsided. Complete recovery from the arthritis occurred in all cases.

The mortality rate was 8 per cent, the meningitis in all but 1 of the 6 fatal cases being of the Waterhouse-Friderichsen type. Four children with this syndrome survived.

GUTTMAN, Philadelphia.

HIGH ALTITUDE FROSTBITE. LOYAL DAVIS, JOHN E. SCARFF, NEIL RODGERS and MERIDETH DICKINSON, Surg., Gynec. & Obst. **77**:561 (Dec.) 1943.

High altitude frostbite differs from ordinary frostbite in that it is caused by extreme degrees of cold (— 40

to —52 C.), usually lasting only a few minutes, and is associated with varying degrees of anoxemia and ischemia of the extremities. It has a special predilection for the extremities.

The mild form follows the briefest removal of a glove at high altitude, the fingers becoming painfully cold, numb, waxy white and completely insensitive to touch. Recovery after removal to a warmer environment may be slow. Several hours may be required for the fingers to soften, and even then the white, ischemic color may persist for several hours longer. No permanent ill effects result, but paresthesias may persist for days or weeks.

The severe types consist of a wet and dry form and follow more prolonged exposure to cold. The wet form is characterized by multiple small cutaneous blisters appearing simultaneously on the affected part, which rapidly coalesce. These large blisters may contain free fluid, but more often the excessive fluid is held fast in the tissue composing the superficial layers of the skin and resists aspiration by needle and syringe. The blister dries in two to three days, the superficial layers of the skin becoming loose and wrinkled, then dry and hard, finally being thrown off, often as a complete cast of the part. The regenerated skin is shiny and varies in color from dusky pink to dusky blue, the color changing with the temperature of the environment. The part is sensitive to cold, and tolerance to cold is considerably reduced. Anesthesia or hypesthesia and analgesia or hypalgesia may persist for months. Loss of sweating of the part parallels the sensory loss.

The dry form usually results after even more extensive exposure. Instead of the formation of blisters, the finger or hand becomes tense, and the skin assumes a dull, ground glass appearance. The affected part then darkens, and all the tissues shrivel and mummify. Spontaneous amputation occurs in two to three weeks. The proximal phalanx of the finger is never involved unless more distal ones are also affected. The outstanding characteristic of this type of frostbite consists of the selective action on the fingers or toes, with sparing of the face, even if exposed for hours. Direct examination of terminal capillary loops in the finger indicates that acute selective vasoconstriction of the peripheral arterioles is the responsible factor, since the terminal arterioles are well filled with blood while the capillary loops are empty. The first effect of the cold is to damage the endothelium and to increase its permeability, thus permitting an extravasation of plasma or blood, which leads to the wet type of frostbite. More severe damage of the endothelium causes thrombosis, usually at the arteriolocapillary junction, which, then, is the basis of the clinical picture of dry gangrene.

Prophylaxis for this type of injury rests in good measure on the engineer, to prevent as far as possible exposure to cold and risks of general anoxemia. Treatment is still in the investigative stage. It is the authors' opinion that maintaining the affected part at room temperature yielded better results than continued, controlled cooling and gradual thawing of the part. Cooling caused less blistering, but a group so treated complained of more pain and ultimately lost more tissue than the patients exposed immediately to room temperature. Attempts to increase the peripheral blood flow by use of amylnitrite, alcohol, acetylsalicylic acid or glyceryl trinitrate, contrary to expectation, resulted in failures to increase the cutaneous temperature in the extremities tested. Sympathetic block was effective in relieving the peripheral vasoconstriction and in raising the cutaneous temperature of the affected digits in cases of mild frostbite but was entirely ineffective in cases in which thrombosis had already occurred.

SHENKIN, Philadelphia.

CHEMOTHERAPY OF INTRACRANIAL INFECTIONS: V. THE TREATMENT OF STAPHYLOCOCCIC AND PNEUMOCOCCIC MENINGITIS WITH SULFATHIAZOLE AND SULFADIAZINE. W. F. MEACHAM, E. SMITH and C. PILCHER, War Med. **6**:378 (Dec.) 1944.

The authors report the results of treatment of staphylococcic and pneumococcic meningitis in 152 experimental animals with the use of sulfathiazole and sulfadiazine. They found that sulfadiazine was present in much greater concentration in the cerebrospinal fluid after oral administration than was sulfathiazole. Experimental staphylococcic meningitis was not benefited by the oral use of sulfathiazole. The oral administration of sulfadiazine was distinctly beneficial in the treatment of staphylococcic meningitis in dogs. Experimental staphylococcic meningitis was not benefited by the intracisternal administration of suspensions of microcrystalline sulfadiazine. This method of therapy is believed to be harmful. The oral administration of sulfadiazine was decidedly beneficial in the treatment of pneumococcic meningitis. A high concentration of sulfadiazine in the cerebrospinal fluid was found to be essential to recovery in the experiments on pneumococcic meningitis.

PEARSON, Philadelphia.

MENINGITIS DUE TO PS. PYOCYANEA: PENETRATING WOUNDS OF THE HEAD. E. H. BOTTERELL and D. MAGNER, Lancet **1**:112 (Jan. 27) 1945.

Botterell and Magner report a series of 11 cases of meningitis due to Pseudomonas aeruginoso (pyocyanea), in 9 of which death resulted. The patients were men with wounds of the head who were evacuated from France to a neurosurgical hospital in England. In 2 cases it is believed on clinical and pathologic evidence that the intrathecal injection of contaminated penicillin might have been the source of the meningitis. In 9 cases infection of the cerebral wound is believed to have spread to the subarachnoid space or the ventricular system. In 4 of the first 9 cases, the meningitis was secondary to cerebral abscess, and it seemed likely that Ps. aeruginosa was present before admission in 3 of the cases. Cultures in another case yielded organisms from temporal muscle adjoining the subarachnoid space. The source of infection in 4 cases seemed to be cross infection in the hospital, attributed in 3 cases to a tube being left in the wound for the repeated instillation of penicillin.

The authors conclude that the risk of meningitis due to Ps. aeruginosa is minimized by complete débridement and primary closure of penetrating wounds and by avoidance of placing of tubes in wounds for the introduction of penicillin. The intrathecal injection of penicillin should be restricted to the treatment of meningitis; in prophylaxis it should be used with caution. For intrathecal use the authors recommend that penicillin be issued in bottles containing only sufficient solution for single injections.

YASKIN, Camden, N. J.

Diseases of the Brain

DIFFUSE NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S DISEASE) INVOLVING THE BULBAR CONJUNCTIVA: REPORT OF A CASE, WITH LESIONS OF THE SKELETAL SYSTEM AND SKIN, BODILY ASYMMETRY AND INTRACRANIAL INVOLVEMENT. FRANCISCO PÁEZ ALLENDE, Arch. Ophth. **33**:110 (Feb.) 1945.

Neurofibromatosis of the nerves of the periosteum of the orbit may cause subsequent erosion and invasion of the osseous wall, or there may be erosion or thinning of the bones through the mechanical effect of pressure on the part of the tumor. Three clinical forms of neurofibromatosis may exist: (1) predominant invasion of the central nervous system (intracranial organs); (2) predominant invasion of external structures (skin), and (3) involvement chiefly of the skeletal system.

When the ocular apparatus and the ocular adnexa are affected, the parts most frequently attacked are, first, the eyelids and the optic nerve, followed by the orbit, the retina, the iris, the cornea, the tarsal conjunctiva and, finally, the bulbar conjunctiva.

The study of the case reported revealed: (1) twinship, (2) coexistence of neurofibromatosis and epilepsy, (3) bodily asymmetry, (4) intracranial disorders, (5) skeletal lesions, (6) cutaneous tumors, (7) partial alopecia of the scalp on the side of the affected eye and (8) slight mental retardation.

SPAETH, Philadelphia.

TOXOPLASMOSIS: REPORT OF OCULAR FINDINGS IN INFANT TWINS. PARKER HEATH and WOLFGANG W. ZUELZER, Arch. Ophth. **33**:184 (March) 1945.

Toxoplasmosis is a recently recognized infectious disease in human beings. Four principal types have been reported: (1) a granulomatous encephalitis, usually of congenital origin and occurring in fetal or early infantile life; (2) an acquired acute encephalitis, occurring in children; (3) an acquired acute disease resembling Rocky Mountain spotted fever, occurring in adults, and (4) a latent subclinical form, occurring in adults.

Heath and Zuelzer report the ocular changes associated with the disease in premature identical Negro twins. The symptoms appeared on the third day after birth. One of the babies died at the age of 1 month. The histopathologic observations on this twin are presented in detail. The second infant lived and was followed through the seventh month after birth. These 2 cases, in which the ocular lesions were so characteristic of toxoplasmosis, gave opportunity for study of the changes seen with the ophthalmoscope in identical twins.

SPAETH, Philadelphia.

THE CEREBROSPINAL FLUID IN METASTATIC BRAIN TUMORS. EDWARD W. SHANNON and CLINTON W. MORGAN JR., New England J. Med. **231**:874 (Dec. 28) 1944.

Shannon and Morgan report on determinations of the protein content of the lumbar cerebrospinal fluid in 43 patients with metastatic intracranial neoplasms. The average protein value was 99 mg. per hundred cubic centimeters. Ninety-one per cent of the patients had a protein value of 40 mg. The highest protein content was found in patients who had superficial cerebral metastases. When supratentorial metastases were present the protein content of the lumbar cerebrospinal fluid was greater than that found in the presence of infratentorial lesions.

The authors conclude that the protein content of lumbar cerebrospinal fluid alone does not differentiate a metastatic neoplasm from a primary tumor of the brain.

GUTTMAN, Philadelphia.

ONE ASPECT OF THE POSTTRAUMATIC SYNDROME IN CRANIOCEREBRAL INJURIES. KENNETH G. MCKENZIE, Surg., Gynec. & Obst. **77**:631 (Dec.) 1943.

McKenzie proposes the hypothesis that the vasomotor system is injured in craniocerebral accidents and is unable to regulate the supply of blood to the brain and that post-traumatic complaints of dizziness, light-headedness, black-outs, headache and mental and physical fatigue result. A case is cited of a young man who six months after a head injury and a period of unconsciousness lasting one-half hour complained of persistent incapacitating headache and dizziness. The dizziness proved to be faintness or light-headedness on change from the horizontal to the erect position. The systolic pressure was 120 mm. of mercury with the patient in the horizontal position; in the standing position the pulse disappeared at the wrist, and the patient became white and nearly fainted. Adaptation to the new position required a few moments. Sleeping with the shoulders and head up and practice in stooping exercises resulted in complete relief from symptoms in three months.

The author now has patients sitting up and out of bed as soon as possible after an injury to the head, usually in a few days. This, he feels, more quickly retrains the injured vasomotor system to meet the demands of variation in posture. In addition, early mobilization of the patient indicates that progress is being made and minimizes the effects of the injury to patient and relatives, thereby having a favorable psychologic influence on the situation. The author further suggests that hospitalization be prolonged for patients with post-traumatic complaints of this nature and that active treatment be carried out. Such therapy consists of stooping exercises, games requiring changes of position and occupational therapy, all given with a view to retraining the vasomotor system.

SHENKIN, Philadelphia.

DEJERINE-ROUSSY SYNDROME CAUSED BY GUNSHOT WOUND: REPORT OF A CASE. PEDRO I. LANZANI and F. DE GREGORIO LAVIÉ, Prensa méd. argent. **46**:2338 (Nov.) 1944.

The authors report the second case of thalamic hyperesthetic anesthesia, or the Dejerine-Roussy syndrome, caused by a gunshot wound. A 20 year old Argentinian woman was admitted in a state of shock with two gunshot wounds, one bullet lodging in the region of the third cervical vertebra and the other entering the left frontoparietal region and lodging finally in the left occipital region. On the fourth day, aphasia was noted, and the right corneal reflex was diminished. On the eighth day the disks were blurred. In about three months a hemisensory syndrome was found on the right side, with absence of the plantar response on that side. There were also some alexia and agraphia. Two months later, headache and dizziness were intense, and the patient became excited. Bilateral papilledema was found, with pronounced diminution of vision in the right eye. Taste, smell and hearing sensations were diminished on the right side. There was dystereognosis on the same side, as well as global aphasia. The patient was operated on four months after the injury, and a temporal decompression

was done on the right side. The signs of increased intracranial pressure disappeared. There was no real thalamic pain, and no thalamic dysesthesias were noted. At the end of nine months there was no longer motor weakness and the aphasia had disappeared; there was diminished sensation on the right side of the body, with sensory changes in the first division of the left fifth nerve.

SAVITSKY, New York.

Encephalography, Ventriculography, Roentgenography

ROENTGENOLOGIC MANIFESTATIONS AND CLINICAL SYMPTOMS OF RIB ABNORMALITIES. HOWARD A. STEINER, Radiology **40**:175 (Feb.) 1943.

Steiner studied 38,105 roentgenograms of the spine, chest and abdomen. Among this number were 59 (0.15 per cent of the total) with abnormalities of the ribs. These anomalies are classified as follows: (1) cervical ribs; (2) lumbar ribs; (3) bipartition of ribs or forking of the anterior end; (4) synostosis, or bony union of adjoining ribs; (5) "tile roof" ribs, or imbrication of ribs; (6) rudimentary ribs, and (7) other deformities.

Nineteen cases of cervical ribs, or 32 per cent of the 59 cases, were noted. In all these the anomaly was associated with the seventh cervical vertebra. In 2 cases the condition was bilateral. The average length of the cervical ribs on the right side was slightly greater than that of the ribs on the left (44.4 mm., as compared with 37.5 mm.). The longest cervical ribs were of the joined type, and their incidence was about equal to that of the unjoined ribs.

The association of roentgenographic evidence and of symptoms was stated as follows: (1) very positive correlation; (2) slightly positive correlation, and (3) negative correlation. The chief complaint was pain, which was present as a positive correlation in 10 cases, or 52.6 per cent. In 6 cases the pain was localized to the back of the neck, and in 4 cases it was referred to the shoulder or to the supraclavicular region. No instance of neuromuscular disturbance of the hands or arms was noted. In 3 cases, or 15.9 per cent, vague pain was localized to the shoulder joint, suggestive of bursitis. In the remaining 6 cases, or 31.5 per cent, no symptoms were referable to the cervical ribs. Thus, in 68.5 per cent of the cases of cervical rib symptoms were associated with the anomaly. Age appeared to be of no significance. Two thirds of the patients were females.

Seventeen cases of lumbar rib were found, the condition being bilateral in all but 1 case. All of these were associated with the first lumbar vertebra. In 12 cases the anomaly was associated with symptoms, backache, of varying degrees of severity, being complained of in all. As in the cases of cervical rib, there was a predominance of females (12 females to 5 males).

In 5 cases bifurcation of the ribs was present; in 2 cases the first ribs were involved and in 2 the fourth ribs. In 1 of the cases an apical tuberculous lesion was demonstrated. Schedtler found that abnormalities of the first rib predispose to apical tuberculosis. Four, or 80 per cent, of the patients with this abnormality were males.

Synostosis was present in 5 cases. In 3 cases the union was between the first and the second rib; in 2 cases a tuberculous lesion was present in the apex of the lung behind the synostosis. In the other 3 cases there was no correlation of symptoms. All 5 patients were males.

"Tile roof" formation, or imbrication of the ribs, was present in 4 cases, in 3 of which the condition was bilateral. In 3 of the 4 cases pneumonia or tuberculosis was the chief clinical symptom. In the fourth case there was a chronic cough but no definite pulmonary lesion. Three of the patients were males.

In 5 cases a rudimentary rib was found, the anomaly being always confined to the first rib. In 3 cases the lesion was bilateral. No symptoms were associated with this abnormality. Four of the patients were males.

In 4 cases other deformities not falling into the preceding classification were observed, all of different types. None of them were associated with symptoms.

KENNEDY, Philadelphia.

DEVELOPMENTAL THINNESS OF THE PARIETAL BONES. JOHN D. CAMP and LEO A. NASH, Radiology **42**:42 (Jan.) 1944.

The authors discuss the salient features of parietal thinness on the basis of a study of 119 cases. This condition, known to anatomists and pathologists, escaped the attention of roentgenologists until 1910.

Two types of parietal thinness of the skull are seen in the posteroanterior projection—the flat and the grooved. The thinness is greatest at the center of the lesion and decreases as the periphery is approached. The defect is primarily in the diploe, while the outer table is thinned and depressed. The authors, contrary to previous case reports, did not find the inner table affected. In their series, this anomaly was found in 0.46 per cent of all examinations. In the 119 cases, the condition was bilateral in 107, of the flat type in 106 and of the grooved type in 13. In 80 cases females were affected, and the average age was 56; 10 of the patients were under 30 years of age.

No clinical symptoms could be attributed to the lesion of the skull. The cause is unknown, being most likely a diploic dysplasia of developmental origin.

The importance of parietal thinness lies only in differentiating it from somewhat similar-appearing conditions of the skull. Developmental thinness of the parietal bones is unrelated to enlarged parietal foramens.

TEPLICK, Philadelphia.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

PAUL I. YAKOVLEY, M.D., *Presiding*

Regular Meeting, Nov. 16, 1944

Capillaries of the Finger Nail Folds in Cases of Neurosis, Epilepsy and Migraine. DR. ALFRED HAUPTMANN.

I have examined 125 normal persons, 375 neurotic patients, 117 epileptic patients, 37 patients with migraine headache, 21 patients with nonmigraine headache and 28 patients with other neurologic diseases for the morphologic characteristics of the capillaries of the finger nail folds.

Ninety-three per cent of the normal persons had normal capillaries; 7 per cent showed abnormalities of the capillaries such as are seen in neurotic persons. Normal capillaries are hairpin-like; there is visible no subpapillary network of vessels and the network characteristic of the early development of the capillaries in newborn children, and found also in mentally retarded children, is not present.

Eighty-eight per cent of the patients with constitutional neuroses showed abnormal capillaries, and 11.9 per cent only had normal capillaries. On the other hand, of persons with neurotic reactions, that is, with an acquired neurosis, only 4.3 per cent had abnormal capillaries and 95.7 per cent normal capillaries. The most frequent morphologic abnormality of the capillaries was tortuosity. Another abnormality was the unequal distribution of the capillaries in one horizontal line. The corium papillae was not well scalloped. In a small percentage of patients an immature picture, observed in children prior to the final development of the capillaries, was noted. Of 586 subjects, (normal subjects, neurotic patients, patients with nonmigraine headache and persons with other neurologic diseases), this percentage did not exceed 12.4. Patients with anxiety neuroses exhibited the highest percentage of abnormal capillaries. Patients with hysteria had the most immature capillaries.

Thus, the capillary picture permits to a certain extent the differentiation of constitutional neurosis and neurotic reactions (acquired neurosis). It might be a welcome aid in detecting neurotic persons in a group of so-called normal persons, e. g., would-be soldiers at the induction center, employees for special branches in which a stable personality is required or school children.

Of the 117 epileptic patients, 68.4 per cent of the 73 with idiopathic epilepsy showed a horizontal network of vessels in the area proximal to the end row capillaries, whereas only 22.7 per cent of patients with symptomatic epilepsy showed this pattern. This picture must be interpreted as one of immaturity, as standstill in the development of the capillaries before the end point is reached. The fact that the figures are not higher than 68.4 per cent or lower than 22.7 per cent can be explained partly by the difficulty in distinguishing between idiopathic and symptomatic epilepsy and partly by the probability that some of the patients with symptomatic epilepsy actually had potential idiopathic epilepsy. This capillary picture is not absolutely characteristic of epilepsy, since some neurotic persons, and even some normal persons, show the same pattern; however, the low percentage (12.4) found in those people differs widely from the high percentage (68.4) for the epileptic patients.

I should not say that the presence of a horizontal network of vessels is a positive diagnostic aid in questionable cases of epilepsy; however, the absence of this pattern speaks strongly against the presence of idiopathic epilepsy.

Of the patients with migraine, 54 per cent showed the same picture as did epileptic patients, whereas none of the patients with nonmigraine headache had this kind of picture. These findings support the view that epilepsy and migraine are related.

Functional alterations of the capillaries, changes in the blood flow due to emotional stimuli, to hyperventilation, to drugs or to smoking, have been studied in addition to these morphologic abnormalities and will be reported on later.

DISCUSSION

DR. FELIX DEUTSCH: I consider this investigation important, especially with respect to epilepsy. I wish to ask a few questions about the findings in the neurotic patients. In the patients with neurosis on a constitutional basis, what primary changes in the capillary formation should be looked for? Dr. Hauptmann was interested only in the formation of the capillaries and did not discuss the functional behavior of the capillaries. One can find fairly normal capillaries with abnormal function. Therefore, when one examines a neurotic patient, one is concerned not only with the form but with the behavior of the capillaries. In patients with hysteria one finds a primary disturbance, an arrested development, of the capillaries. In patients with obsessional neuroses this functional behavior is not observed so regularly. Why is it necessary to call so much attention to the behavior of the subcapillary plexus? It indicates an arrested development. Secondary formative disturbances must also always be taken into consideration. During life the capillaries may undergo various formative changes; for instance, aged people or people who have high blood pressure may show secondary changes in the capillaries. Therefore, one must always consider what sicknesses the patient had or what drugs he has taken in the past. I want to stress the fact that the formation of the capillaries is not enough for evaluation of their relation to a neurosis but that their behavior must also be examined.

DR. D. DENNY-BROWN: I should like to ask Dr. Hauptmann whether he has observed any relation between these changes in the capillary plexus and the growth of the nails; perhaps this plexus has some relation to the underlying nail bed.

DR. WILLIAM G. LENNOX: Paskind and Brown compared the capillaries of deteriorated and of mentally normal epileptic persons (Constitutional Differences Between Deteriorated and Nondeteriorated Patients with Epilepsy, ARCH. NEUROL. & PSYCHIAT. **49**:49 [Jan.] 1943). The greater distortion of capillaries in the deteriorated group was ascribed to constitutional inborn differences. I wonder whether the form of the capillaries is a hereditary trait. If so, it would be of interest to compare the capillaries of the parents of

these epileptic patients, as well as the loops of identical twins when only one has epilepsy. What about brain waves? Is there any correlation between cortical dysrhythmia and tortuosity of the capillaries?

DR. OSCAR RAEDER: In the family with 2 children, did the father, the son and the daughter all have a neurosis?

DR. ALFRED HAUPTMANN: This paper represents only one part of my study. The function of the capillaries must also be investigated. It is more difficult to evaluate the functional changes than the morphologic. However, the morphologic pattern is as important as the functional behavior. Of course, heart disease, or any other disease, may have an influence on the capillaries, and Müller (Müller, O.: Die Kapillaren der menschlichen Körperoberfläche in gesunden und kranken Tagen, Stuttgart, Ferdinand Enke, 1922) has included a number of pictures of capillary patterns, especially in cases of renal disease. The pictures I have shown here concern patients who have no disease other than neurologic disorders. I found the most immature picture in hysterical patients and the greatest number of tortuosities in patients with anxiety neurosis. Age does not change the morphologic character of the capillaries.

To answer Dr. Denny-Brown, I did not observe the nails especially. One of the residents studied the nails, and he was of the opinion that neurotic patients also show abnormalities of the nails.

To answer Dr. Lennox, in only 3 cases have I had the opportunity of seeing the parents and siblings of epileptic patients. In 1 case, a sister and a brother, without having epileptic fits, had a network of the horizontal variety seen in epileptic persons. In the other 2 cases I did not find any abnormality of the capillaries. Three cases, however, do not mean anything. I did not examine any twins, but I should like very much to do so.

In answer to Dr. Raeder, in the family mentioned, the father, the daughter and the son were all extremely neurotic, and all had highly abnormal capillary patterns.

PHILADELPHIA NEUROLOGICAL SOCIETY

GEORGE D. GAMMON, M.D., *Presiding*

Regular Meeting, Nov. 24, 1944

Curious Lesions of the Spinal Cord: Report of Two Cases. DR. FRANCIS C. GRANT and DR. HENRY SHENKIN.

L. S., a 16 year old boy, noted sixteen months prior to his admission to the neurologic service of the Hospital of the University of Pennsylvania that he was gradually losing power in his left leg. This weakness progressed until his admission to the hospital; in addition, three months before he began to notice weakness in his right leg. At no time had there been any pain or paresthesia. There had never been any difficulty with his sphincters.

The past medical history is of interest in that there had been complete paralysis of both legs of two months' duration at the age of 6 years. The cause was never determined, but the child improved gradually, and up to the time of his present illness he had been completely well. We have a statement from the hospital confirming this record.

Neurologic examination revealed spastic gait, with a tendency to swing the left hip and foot in a hemiplegic manner. The Romberg sign was positive, with a tendency to sway more to the left. The left lower limb was extremely weak and the right moderately weak; both limbs were spastic. All reflexes in the lower limbs were hyperactive; the patellar reflex and the achilles were elicited on both sides. The Babinski sign was present bilaterally. All the abdominal reflexes were absent. There was an indefinite level for pain, touch and temperature sensations at the sixth thoracic dermatome, with sacral sparing. Position and vibration sensations were absent in both lower limbs. The upper limbs and the cranial nerves were entirely normal.

The spinal fluid dynamics were normal except for a partial block in the Queckenstedt test. The total protein was 21 mg. per hundred cubic centimeters.

Plain roentgenograms of the thoracic portion of the spine showed changes in the epiphyses and the bodies of the vertebrae, from the fifth to the twelfth dorsal, commonly associated with Scheurerman's disease. The intervertebral pedicular measurements were normal. A myelogram obtained after cisternal injection of Pantopaque (an iodized poppyseed oil) showed a block at the fifth thoracic interspace. The lesion was suspected of being a spinal extradural cyst, although the typical fusiform spreading of the vertebral pedicles was lacking. The possibility of an intramedullary tumor of the cord was also entertained. In any event, operation was clearly indicated.

A laminectomy was performed on Nov. 4, 1944. A white, shiny, intramedullary lesion, which did not seem to be well demarcated from the cord, was exposed at the level of the fifth thoracic vertebra. An incision was made through the pia parallel to the long axis of the cord; it included possibly a very thin layer of the posterior column, although it was doubtful whether there was much cord substance at this point. When the incision was made, there began to extrude the white, soapy, greasy material characteristic of an epidermoid. The cavity was well opened, and all its contents were carefully removed. A small piece of the capsule was also removed for verification. The cavity seemed to involve most of the left half of the cord. The patient has done well since operation. He voided spontaneously from the first and was up and walking on the twelfth postoperative day.

Microscopic examination of the section of the cyst wall showed a typical band of stratified squamous epithelium resting on a narrow layer of connective tissue. Keratinized epithelial debris was everywhere present. There was no evidence of accessory structures of the skin.

Epidermoid cysts of the spinal canal are rare tumors and apparently arise from misplaced rests of epithelial tissue, probably due to improper separation of neuroectoderm from surface ectoderm. It is interesting to note that this boy had complete paraplegia at the age of 6 years, which underwent complete remission in two months. In view of the congenital nature of the tumor, it is not too much to assume that this paraplegia was related to the lesion removed ten years later.

M. F., a previously healthy, 20 month old child, was first seen at the Children's Hospital on June 18, 1943, with a history of irritability and drowsiness of one week's duration. Examination at that time showed high fever and cutaneous lesions of a papular nature scattered over the arms and legs. The child was admitted to the hospital with a diagnosis of erythema multiforme or septicemia. (Lumbar puncture revealed nothing abnormal except for a total protein content of

250 mg. per hundred cubic centimeters. Three weeks later the tap was repeated, and the total protein then measured only 20 mg. per hundred cubic centimeters. The cutaneous lesions cleared; the child's condition improved; he ate well and became more active. He was discharged on July 7, 1943.

However, ten days later, on July 17, he again became irritable and restless and refused to walk or stand. Examination at this time showed marked ataxia of the lower extremities, exaggerated patellar reflexes and suggestive cervical rigidity. Lumbar puncture revealed clear fluid, a pressure of 85 mm. of water and a cell count of 3 leukocytes per cubic millimeter. The Queckenstedt test showed partial block, and the total protein measured 400 mg. per hundred cubic centimeters.

Eight days after his second admission there developed a persistent ankle clonus and a bilateral Babinski sign. Injection of iodized poppyseed oil into the cisterna revealed a block at the level of the fourth thoracic vertebra.

The child subsequently had complete paraplegia with hyperactive reflexes; ankle clonus and the Babinski sign were present bilaterally. No sensory changes were demonstrable. With the patient under ether-procaine anesthesia, the laminas of the fourth, fifth, sixth and seventh thoracic vertebrae were removed. The laminas of the sixth and seventh vertebrae were removed first. The epidural fat had a greenish orange color, with apparent disappearance of the dura itself in this region. Under the lamina of the fifth thoracic vertebra the end of a mass lesion which seemed to involve the dura was disclosed. The bones of the fourth and fifth thoracic vertebrae were carefully removed; there was complete absence of the epidural fat, and a curious, greenish, soft, fluctuant lesion appeared. The lesion appeared to extend upward just under the lamina of the third thoracic vertebra. The more the lesion was exposed, the greener and more apparently cystic it became. While better exposure was being obtained, in order to make a photograph, it was noticed that the lesion itself was becoming less prominent. The reason was that a brownish, gelatinous, coffee-like material was draining from its upper end. With the escape of this fluid, the cyst collapsed, before a satisfactory color photograph could be obtained. The lesion definitely involved the dura, which was removed with the cystic mass. It seemed to lie between the layers of the dura. Removal of the lesion was complete.

Convalescence was relatively uneventful, and on his discharge, three and one-half weeks after operation, the child was able to walk with assistance. When he was last seen, six months after operation, he was able to walk and run about normally.

The microscopic appearance of the specimen removed at operation was typical of the subdural hematomas occurring in the intracranial cavity. It consisted of a connective tissue membrane, the inner portion of which was a relatively loose meshwork containing many dilated, thin-walled capillaries filled with blood. The outer portion of this membrane was composed of denser fibrous tissue and was limited by a single layer of flattened cells. Blood pigment was scattered throughout the inner portion of the membrane.

A fairly complete survey of the literature failed to reveal any similar case. However, in our own collection, we have 2 cases of epidural bleeding, both in adults, in 1 of which the lesion was definitely related to trauma, without fracture of the vertebrae. In this case, in which operation was performed eighteen hours after the trauma, no membranes were found. In the first case, there was no definite history of trauma, and a hematoma with membrane was observed.

The origin of the hematoma reported here is not clear. There was no history of trauma. It would appear that the bleeding was spontaneous and was related to a systemic, infectious process. The nature of the lesion, however, cannot be doubted, in view of its pathologic appearance and the subsequent full recovery of the child on its removal.

DISCUSSION

DR. HENRY T. WYCIS: I should like to ask Dr. Grant how frequently he thinks such epidermoid tumors occur. Has he encountered any other cases? I recall only 1, that of Dr. Fay, and in this case an epidermoid filled the entire sac.

DR. GEORGE D. GAMMON: I should like to ask whether the preceding paralysis, such as occurred in this case, is commonly associated with epidermoid cysts. My associates and I were puzzled how to explain the paraplegia which the youngster had ten years before his second attack of paraplegia. He was admitted to the Tuberculosis Hospital at Mount Alto, Pa., but apparently no evidence of tuberculosis was found at that time.

DR. B. J. ALPERS: Was there any connection with the meninges in the second case? I do not know of any instance in which a cerebral epidermoid has been intramedullary. There are epidermoids in the skull, and epidermoids of the brain are entirely extramedullary. One of the interesting features of this case is the intramedullary character of the tumor. I wonder whether the tumor was one which had pushed its way into the substance of the cord or whether it was in fact a medullary tumor. I raise this question because epidermoids should arise from extramedullary sources rather than within the brain substance itself.

DR. MICHAEL SCOTT: I should like to ask Dr. Grant whether any thought was given to the possibility of the presence of typical scurvy, vitamin C deficiency or any type of blood dyscrasia in the first case.

DR. FRANCIS C. GRANT: As to our experience with epidermoids of the spinal cord, I can state that this is the only case I have ever seen of a tumor of this type in the spinal cord. I can give no details, therefore, as to the duration of symptoms except in this particular case.

The tumor lay, as far as I could judge, beneath the pia. Certainly, there was a fine, tough membrane over the surface of the tumor which had to be sectioned before intracapsular removal was possible. This membrane may have been the pia, or it may have been the capsule of the tumor. The microscopic sections may throw light on this point.

With regard to the hemorrhagic lesion in the first case, which both from the position at operation and from pathologic evidence seemed to be an intradural blood clot, no evidence of either scurvy or blood dyscrasia was noted, and there was no history of antecedent trauma. In 2 previous cases in our records, in which the bleeding was obviously epidural, there was a history of trauma to the spinal column, and in 1 of them there was, in addition, pronounced hypertension.

Function of the Anterior Cerebellar Lobe. DR. GERVASE J. CONNOR.

Within the anterior cerebellar lobe are represented probably all stages of cerebellar development—the archi-

cerebellum, the paleocerebellum and the neocerebellum. In the dog ablation of this region provokes a profound extensor release in the antigravity muscles, of such a character that these muscles become abnormally responsive to extensor postural influences, whether of local, segmental or general static nature. This leads to strongly hyperactive reflexes of stance, incoordination in all the extremities, hyperactive and spreading deep tendon reflexes and well defined lengthening and shortening reactions, or plasticity.

In the single case of a tumor of the anterior cerebellar lobe in man, signs of a similar, but more subtle, nature are observed. It is not so much the local postural responses themselves as their susceptibility to modification from segmental and suprasegmental sources that characterizes this syndrome.

There is evidence to suggest that within the anterior cerebellar lobe there is resident a discrete type of functional localization, so precise that individual extremities and the labyrinths are specifically represented.

DISCUSSION

DR. HENRY T. WYCIS: I should like to ask Dr. Connor two questions: First, what are the probable compensatory mechanisms which account for the waning of the exaggerated postural reactions following ablations of the anterior lobe? Second, what is the influence of bilateral labyrinthectomy on the postural reactions appearing after ablation of the anterior lobe?

DR. HENRY SHENKIN: I have had no experience with this region, but I should like to ask whether Dr. Connor noted any sensory changes in his animals with ablations of the anterior cerebellar lobe. There are some isolated reports by other investigators of sensory changes observed in cerebellar preparations.

DR. GEORGE D. GAMMON: I should like to ask Dr. Connor about the time course of these various phases and what the ultimate condition is. How rapidly do these animals recover? Is the first phase described as the "exaltation" of Luciani?

LIEUT. COMDR. WILLIAM GERMAN (MC), U.S.N.R.: I should like to comment on some of the clinical aspects that Dr. Connor mentioned. The case I shall describe presented the puzzling problem of a patient who appeared to have a cerebellar lesion; yet, because of the positive nature of his ataxia, I was inclined to think that the lesion was a contralateral frontal one. In other words, he did not fall to the side; he pushed himself over to one side. It was just as Dr. Connor described it—an excessive support reaction. His process of standing was a caricature of excessive standing. In fact, he stood so hard on the affected side that he pushed himself over to the other side, and in walking he progressed in the same manner. I have never seen such forced ataxia except with frontal lesions.

The patient had given a history of gradually progressive disability over a long period, with few or no signs of increased intercranial pressure, and it was not until my colleagues and I had made an injection of air that we were quite certain that his lesion was in the left cerebellar region. It turned out to be as Dr. Connor might have predicted had he seen the patient before the operation. The tumor, in the left anterior cerebellar lobe, was of hemangiomatous origin.

After the operation, Dr. Connor reviewed the situation with us and demonstrated the postural tonic changes which occurred in the reflexes and in the extensor rigidity. There was a striking relaxation of extensor tonus in the left lower extremity when the patient's head was turned to the middle or away from the side of the lesion. When his chin was turned to the side of the lesion, a sustained ankle clonus was elicited on the left. Similarly, when the head was turned to the side of the lesion, there was a very active knee jerk on the same side. The extremity would tend to remain in a position of extension and then gradually drop. I have seen no other cases in which these signs were brought out so strikingly, but perhaps it was because I did not know what to look for. One does not see tumors in this location frequently. It would seem that at least part of this picture should be found in cases of tumors of the cerebellopontile angle. Perhaps it is masked by some of the other effects present.

DR. GERVASE J. CONNOR: I do not know whether sensory disturbances were present. Various sensory examinations were carried out, but the results were not sufficiently accurate in the animal to permit a conclusion.

One of the most interesting parts of the study concerned the effects of labyrinthectomy on the anterior cerebellar syndrome. I purposely omitted discussion of this subject in order to avoid confusing the picture. From a functional viewpoint, one should regard the anterior lobe as a crossroads of the vestibular and the spinocerebellar system. These systems exert a conspicuous effect on the postural pattern. When the labyrinths are removed during the early postoperative period after anterior decerebellation, there is lessening of the extreme extensor dominance, but the extensor muscles in the extremities remain abnormally responsive to local and sequential static influences. It would appear that the fundamental physiologic effect in the extremities after removal of the spinocerebellar portion of the anterior lobe is equivalent to the partial deafferentation of these extremities, the stretch reflex arc remaining intact. Removal of the vestibular portion of the anterior lobe would seem to result in a parallel effect on the labyrinths. This concept would be entirely consonant with Sherrington's oft repeated parallel between the labyrinths and the proprioceptive mechanism in the extremities.

It is difficult for me to be as specific as I should like in answer to Dr. Gammon's question. The time course of the various phases is sharply dependent on the completeness of the ablation. Even small residual areas of cortex are important in this connection. I did not emphasize the time relationships of the various phases in the dog because they are of so much less practical significance than is the composite postural picture. The extreme extensor exaltation, similar to that described as the "exaltation" of Luciani, may last for several weeks, depending on one's definition of the term. Its temporal limits are not easily defined because the exaggerated standing is evident as soon as the animal can get to its feet. Thereafter the phases in recovery merge smoothly one into the other. In the monkey, the phase of extreme extensor exaltation is not very conspicuous. In the anterior decerebellate monkey the extensor exaltation does not completely dominate the mechanism for stepping, even though the positive supporting reaction is exaggerated.

The compensatory postural mechanism may well reside in part in the extrapyramidal system in the cerebral cortex. One would expect a certain amount of encephalization of anterior cerebellar function in animals higher than the dog.

CINCINNATI SOCIETY OF NEUROLOGY AND PSYCHIATRY

ALPHONSE R. VONDERAHE, M.D., *Presiding*

Regular Meeting, Dec. 18, 1944

Studies on Flying Personnel with Operational Fatigue: II. Modification of Pentothal Therapy. LIEUT. COL. BENJAMIN H. BALSER, Medical Corps, Army of the United States.

Recently a group of patients with operational fatigue were treated at a regional station hospital. Intravenous pentothal therapy was used, and in several instances it was noted that the patients failed to improve with it. A recording device was obtained, and with the patients under the influence of pentothal (in a hypnotic state) their productions were recorded on a radio recorder, a hand microphone being used. While the patients were under pentothal narcosis, they spoke freely and vividly of their emotion-laden experiences in the various theaters of combat. However, on recovering consciousness they remembered little of their production. On the day following the treatment and recording, the patients were brought into the office and their records played back to them. The response was dramatic. They went through a tremendous anxiety reaction, during which they perspired freely, were tearful, showed tremors of the jaw, hands and body, sat with their hands and fingers clenched tightly and were obviously under extreme emotional stress. After this, each patient's illness was discussed with him, and he was given an opportunity to return for further discussions, at his own request.

With this form of treatment, these patients responded quickly, and much more rapidly than they did without the use of this mechanism. Final proof of such recovery was evidenced in the ability of a group of these patients to make humorous records similar to, yet mimicking, the productions that they had made while under pentothal hypnosis.

DISCUSSION

DR. CHARLES D. ARING: This is a provocative contribution to the manifold technics known as psychotherapy. This seems to offer another glimmering of hope that the tedious process of psychotherapy may eventually be shortened, as it must be to prevent collapse under its own weight.

Fully cognizant of the fact that one rarely sees in civilian practice the type of patient described by Major Balser, one wonders, nevertheless, whether certain psychologic disorders in civilian life might not lend themselves to pentothal therapy or its modification. The civilian neurosis is engendered a bit differently than the war neurosis. It is almost always the product of a long series of what are to the patient traumatic episodes. The period of development of the military psychologic disorder is compressed by stimuli that are comparatively tremendous, though they impinge on persons who had undergone a certain selection.

A reasonable solution to the impasse that now exists in handling the countless cases of curable psychologic illness would appear to be the introduction of shortening technics. Possibly the war will render one of its few services by forcing their development more quickly than would otherwise have occurred.

DR. MILTON ROSENBAUM: I predict that the method will not hold up in civilian psychiatric practice unless there has been relatively recently a traumatic precipitating event. Psychiatrists have been using pentothal for the post-traumatic neuroses. I remember particularly one patient, a young man in whom a neurosis had developed after an automobile accident three years before, in which a girl companion was killed. This man was married, with several children. My associates and I discussed this girl with the patient but were able to obtain only the most desultory statements about her. With the use of pentothal we learned that the girl was married and that the patient and she were in love. He had broken off their affair, but she had somehow managed to meet him and during this automobile ride had told him of her love for him and her desire, after their respective divorces, for them to marry. He had the instant thought that he must be rid of her, and the accident followed immediately. With the careful use of this material, obtained with the patient under pentothal therapy, it was possible to rehabilitate him.

Several years ago David Lewy described what he called release therapy. He worked with young children who presented symptoms of anxiety of relatively short duration. Using play technics, he allowed the child to "act out" the situation which had precipitated the acute behavior disorder. In the "acting-out" process there was a good deal of emotional release. However, this method was helpful only in those cases in which there had been a relatively recent traumatic event. In cases of the more chronic type intensive psychotherapy was needed.

I think that some of the problems in the treatment of acute battle neurosis and civilian neurosis are indicated by Lewy's work. When a neurosis is precipitated by a recent and intense traumatic event which is then suppressed, use of pentothal is indicated. However, the usual civilian neurosis has no such dramatic start; indeed, the precipitating event is usually so well hidden that it is overlooked, and the etiologic factors have been operating over a long period.

DR. ALPHONSE R. VONDERAHE: May any one have operational fatigue?

MAJOR BENJAMIN H. BALSER, Medical Corps, Army of the United States: It is probable that any one may have operational fatigue. Capt. David Wright has published some observations on this matter. In a study of a group of 150 men who had finished their tour of duty without obvious psychologic disorder, he found that about 95 per cent had symptoms of operational fatigue, which in about a third of them were severe.

DR. HOWARD D. MCINTYRE: How long will the patients talk when under pentothal narcosis?

MAJOR BENJAMIN H. BALSER, Medical Corps, Army of the United States: As long as one will permit. One usually allows a period of ventilation and then ends it by saying, "All right; that's enough. Now you can go to sleep." The patient will sleep about fifteen or twenty minutes and then be up and around.

With the patients who had not responded to ordinary pentothal therapy and to whom the voice records were played back, I usually waited three to five minutes after the record had finished to begin my talk. Only one session was required. I did not know what I was going to meet. Psychotherapy was on a most superficial level. I talked softly and explained to the patient that he was completely normal before the grafting of this illness on his normal personality and that the illness was as he described it himself in the phonograph record. With these 12 patients only one phonograph recording was required to effect an apparent recovery. The men were then transferred to a rest camp, and I do not know their adjustment thereafter.

In ordinary pentothal therapy the first session may require administration of more of the drug than subse-

quent ones, and more stimulating words may be necessary to start the patient talking. A trigger word may be the name of a city which was the goal of a bombing expedition, or it may be the wife's name. These stimuli start talk, and it usually continues until the therapeutist terminates the interview.

During the injection of pentothal, which is done slowly, the patient is asked to count backward from 100. When he begins to mix figures, the end point is reached. This phenomenon is usually followed by nystagmus and then by pseudobulbar speech.

My associates and I have had no improvement with continuous narcosis, contrary to the reports from England. This may be due to the factor of the delay in these patients reaching us.

Capt. Joseph Lander, Medical Corps, Army of the United States: Col. Roy Grinker has a unique setup in Florida, where most of the patients have rather severe combat fatigue. The rate of return of fliers to combat flying is not high, though many are restored to other types of duty.

Grinker stresses the use of the "twilight state" as the patient emerges from pentothal narcosis for the giving of much reassurance and treatment; impressions gained by the patient at this time are of considerable effect.

It is the feeling of some workers that if one were to spend hours with the patient one could achieve about as much as one does with pentothal, but pentothal therapy is a short cut. There are advantages and disadvantages to the use of such a short cut. It saves a great deal of time and produces prompt results. On the other hand, the elimination of a cooperative ego means that the therapeutic result is likely to be less lasting than it would if the total personality participated in the treatment. When one has the "whole personality" working with one, the cathartic and insight values are assimilated far more thoroughly.

However, the primary concern of the Army is a quick and wholesale rehabilitation; for this reason, among others, pentothal treatment is an extremely valuable procedure.

Another point to be borne in mind is that treatment on the spot, a few days after the onset of the disturbance, is likely to be far more effective than that administered months, and sometimes a year, after the syndrome has appeared and become relatively fixed. For this reason, I expect that the results of pentothal treatment overseas will be far more encouraging than here.

Dr. I. Mark Scheinker: I wonder whether the beneficial and prompt results obtained with the method developed by Major Balser would not warrant the drawing of a certain parallelism with those results Freud obtained in his early period of psychotherapy. In his protocols, Freud described the immediate dramatic effect obtained in a series of cases through a hypnotically induced "revival" of the psychogenic trauma.

Book Reviews

The Basis of Clinical Neurology. By Samuel Brock, M.D. Second Edition. Price, $5.50. Pp. 393, with 72 illustrations. Baltimore: Williams and Wilkins Company, 1945.

It is hard to believe that the first edition of Dr. Brock's book was as recent as 1937 in view of its wide acceptance and of the numerous generations of medical students brought up in its tradition. One is not surprised to learn from the present edition that the text has been translated into Portuguese, for it is truly a one volume encyclopedia of applied neuroanatomy and neurophysiology.

It is an axiom that in a work of this kind there are many subjects which cannot receive full consideration; emphasis must be the more or less arbitrary prerogative of the author. While a section on electroencephalography has been added by Dr. Paul F. A. Hoefer, the rising importance of this technic in present day neurology would merit more space. A section by Dr. Joseph Moldaver on electrodiagnostic methods is included, and Dr. Irving Simons has revised the section on urination.

The book is of sufficiently excellent quality that the reviewer may freely make suggestions without impugning its essential value. Especially could one wish for an amplification of the index, which is much too brief. In addition, the bibliography is awkwardly arranged. Divided as the list is into sections which follow groups of allied chapters, one is forced to leaf back and forth for the necessary connections. It would be much better to have the complete bibliography at the end. Furthermore, the additional use of fine print would increase the readability of the text; too much detail in the body spoils it for rapid review, and the style is rather pedestrian.

Dr. Brock's book, in its first edition, won its place. The second edition continues to be indispensable.

News and Comment

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES

The trustees of the Association for Research in Nervous and Mental Diseases have voted to postpone the next meeting of the association, usually held in December, for a year. The subject for discussion will be "Epilepsy."